



REFERENCE ONLY

UNIVERSITY OF LONDON THESIS

Degree *phd*

Year *2006*

Name of Author *ROTHSTEIN, V*

**COPYRIGHT**

This is a thesis accepted for a Higher Degree of the University of London. It is an unpublished typescript and the copyright is held by the author. All persons consulting the thesis must read and abide by the Copyright Declaration below.

**COPYRIGHT DECLARATION**

I recognise that the copyright of the above-described thesis rests with the author and that no quotation from it or information derived from it may be published without the prior written consent of the author.

**LOANS**

Theses may not be lent to individuals, but the Senate House Library may lend a copy to approved libraries within the United Kingdom, for consultation solely on the premises of those libraries. Application should be made to: Inter-Library Loans, Senate House Library, Senate House, Malet Street, London WC1E 7HU.

**REPRODUCTION**

University of London theses may not be reproduced without explicit written permission from the Senate House Library. Enquiries should be addressed to the Theses Section of the Library. Regulations concerning reproduction vary according to the date of acceptance of the thesis and are listed below as guidelines.

- A. Before 1962. Permission granted only upon the prior written consent of the author. (The Senate House Library will provide addresses where possible).
- B. 1962 - 1974. In many cases the author has agreed to permit copying upon completion of a Copyright Declaration.
- C. 1975 - 1988. Most theses may be copied upon completion of a Copyright Declaration.
- D. 1989 onwards. Most theses may be copied.

*This thesis comes within category D.*

☒

This copy has been deposited in the Library of UCL

☐

This copy has been deposited in the Senate House Library, Senate House, Malet Street, London WC1E 7HU.





**THE NEURAL CORRELATES OF  
EARLY IDENTITY AND  
EXPRESSION PROCESSING**

Pia Rothstein

PhD Dissertation

Wellcome Department of Imaging Neuroscience,  
Institute of Neurology

University College London

UMI Number: U593396

All rights reserved

INFORMATION TO ALL USERS

The quality of this reproduction is dependent upon the quality of the copy submitted.

In the unlikely event that the author did not send a complete manuscript and there are missing pages, these will be noted. Also, if material had to be removed, a note will indicate the deletion.



UMI U593396

Published by ProQuest LLC 2013. Copyright in the Dissertation held by the Author.  
Microform Edition © ProQuest LLC.

All rights reserved. This work is protected against  
unauthorized copying under Title 17, United States Code.



ProQuest LLC  
789 East Eisenhower Parkway  
P.O. Box 1346  
Ann Arbor, MI 48106-1346

## **Abstract**

Faces are probably one of the most important objects that we encounter in that they convey multi-layered and intertwined information such as identity, intentionality and emotional expression. Thus, it is not surprising that understanding a face has been the focus of intense multi-disciplinary research over the last decades.

An influential framework for face processing was suggested by Bruce and Young (1986). Based on this model I tested three hypotheses: the first relates to the hierarchical structure of face processing; the second relates to the nature of early face processing and the third relates to a possible early route for expression processing.

The hierarchical nature of identity processing was tested using fMRI and behavioural experiments. These studies suggested three stages for face identity processing: the first involves representation of physical properties of a face in posterior occipital cortices; the second reflects categorical representation of identity in fusiform gyrus; the third represents facial identity processing that depends on familiarity with a face and involves anterior temporal polar cortices.

Focusing on the first stage of the hierarchical processing of a face, I suggest that in early identity processing different types of information from of a face are processed separately. Two dissociations are observed in posterior occipital cortices, the first between processing different bands of spatial frequency information and the second between processing feature and configural information. In addition, I demonstrated that featural information is important for individuating faces and sensitivity to configural information is predictive of general face recognition skill.

Evidence for early processing of expression information that is mediated via amygdala is demonstrated in a patient study. Patients and healthy controls with intact amygdalae differed from patients with amygdale lesions in an early ERP and fMRI responses to fearful expressions.

## **Table of Contents**

# **PART I: LITERATURE REVIEW AND METHODOLOGICAL BACKGROUND.....11**

## **CHAPTER 1:INTRODUCTION.....12**

### **1.1 Thesis overview.....12**

### **1.2 A frame work for understanding face recognition.....14**

#### *1.2.1 Bruce and Young's (1986) face recognition model.....14*

#### *1.2.2 Bruce and Young's model revisited.....16*

#### *1.2.3 Anatomical models for face processing.....16*

##### *1.2.3a Neuropsychological model.....16*

##### *1.2.3b Distributed neural network of face processing.....19*

#### *1.2.4 Functional and anatomical predictions based on the above models.....21*

### **1.3 Cognitive psychology research.....23**

#### *1.3.1 Evidence for hierarchical structure.....23*

#### *1.3.2 Dissociation of familiar and unfamiliar faces.....24*

#### *1.3.3 Are expression and identity process in parallel?.....25*

### **1.4 Neuropsychological research.....25**

#### *1.4.1 Prosopagnosia – historical background.....25*

#### *1.4.2 Anatomical-function relation.....27*

#### *1.4.3 Dissociation of familiar from unfamiliar faces .....31*

#### *1.4.4 Dissociation of expression, age, gender from identity processing.....33*

### **1.5 Electrophysiology research in monkeys.....35**

#### *1.5.1 Face selective cells in monkey's IT.....35*

#### *1.5.2 Dissociation of familiar from unfamiliar faces.....37*

1.5.3	<i>How does the brain dissociate between expression and identity processing.....</i>	38
1.5.4	<i>Face selective cells outside the visual ventral stream.....</i>	39
<b>1.6</b>	<b>Electrophysiological research in human.....</b>	<b>40</b>
1.6.1	<i>Single cell recording in humans.....</i>	40
1.6.2	<i>Evoked Response Potentials (ERPs) of face processing.....</i>	42
1.6.2a	<i>N170.....</i>	42
1.6.2b	<i>300 – 600msec post stimuli onset.....</i>	44
1.6.2c	<i>P1/N1/M1.....</i>	45
1.6.2d	<i>Summary.....</i>	45
<b>1.7</b>	<b>Neuroimaging research.....</b>	<b>46</b>
1.7.1	<i>Are identity processes hierarchical?.....</i>	46
1.7.2	<i>The role of fusiform gyrus.....</i>	47
1.7.3	<i>Face identity processing beyond the FFG .....</i>	48
1.7.4	<i>Representation of familiar and unfamiliar faces.....</i>	49
1.7.5	<i>Dissociation between expression and identity.....</i>	50
<b>1.8</b>	<b>Summary.....</b>	<b>51</b>
<b>Chapter 2:</b>	<b>Functional Magnetic Resonance Imaging.....</b>	<b>53</b>
<b>2.1</b>	<b>Introduction.....</b>	<b>53</b>
<b>2.2</b>	<b>Data acquisition: MRI.....</b>	<b>54</b>
2.2.1	<i>Magnetic field.....</i>	54
2.2.1a	<i>Spin – T1.....</i>	54
2.2.1b	<i>Spin precession, phase – T2.....</i>	55
2.2.2	<i>Radio frequency pulse.....</i>	56
2.2.2a	<i>T1 relaxation.....</i>	57
2.2.2b	<i>T2 &amp; T2* relaxation.....</i>	58
2.2.3	<i>Receiver coils and tissue contrast.....</i>	59
2.2.3a	<i>T1 weighted image.....</i>	60
2.2.3b	<i>T2* weighted image.....</i>	62
2.2.4	<i>Image reconstruction: encoding spatial information.....</i>	62
2.2.5	<i>Echo planner imaging (EPI) – the BOLD.....</i>	66

2.2.6	<i>The origin of the BOLD response.....</i>	67
2.2.7	<i>Artifacts in MRI.....</i>	70
<b>2.3</b>	<b>Using fMRI for cognitive neuroscience research: pros and cons.....</b>	<b>71</b>
2.3.1	<i>Safety issues.....</i>	72
2.3.2	<i>Spatial resolution.....</i>	72
2.3.3	<i>Temporal resolution.....</i>	73
<b>2.4</b>	<b>Analysis of functional MRI time series.....</b>	<b>73</b>
2.4.1	<i>Image pre-processing.....</i>	74
2.4.1a	<i>Spatial realignment and unwrapping.....</i>	74
2.4.1b	<i>Temporal realignment .....</i>	76
2.4.1c	<i>Spatial normalization.....</i>	77
2.4.1d	<i>Spatial smoothing.....</i>	79
2.4.2	<i>The general linear model.....</i>	79
2.4.2a	<i>Design matrix and contrasts.....</i>	80
2.4.2b	<i>Comparison across subjects – random effect analysis.....</i>	83
2.4.2c	<i>Classical statistical inferences.....</i>	84
<b>2.5</b>	<b>Experimental design .....</b>	<b>85</b>
<b>CHAPTER 3:</b>	<b>ELECTROENCEPHALOGRAM IMAGING.....</b>	<b>89</b>
<b>3.1</b>	<b>Introduction.....</b>	<b>89</b>
<b>3.2</b>	<b>The source of scalp electronic current.....</b>	<b>89</b>
<b>3.3</b>	<b>Data acquisition – EEG.....</b>	<b>92</b>
3.3.1	<i>Electrodes.....</i>	92
3.3.2	<i>Reference.....</i>	93
3.3.3	<i>Recording montage.....</i>	94
3.3.4	<i>Amplifiers.....</i>	95
<b>3.4</b>	<b>Using EEG for cognitive neuroscience research: Pros and cons.....</b>	<b>96</b>
3.4.1	<i>Safety issues.....</i>	96
3.4.2	<i>Spatial resolution.....</i>	97
3.4.3	<i>Temporal resolution.....</i>	97
3.4.4	<i>Understanding the signal.....</i>	97

<b>3.5 Data analysis – EEG.....</b>	<b>98</b>
3.5.1 <i>Signal pre-processing.....</i>	98
3.5.2 <i>Event related potential analysis.....</i>	99
3.5.2a First level, single subject analysis.....	99
3.5.2b Second level, group analysis.....	100
<b>3.6 Experimental design.....</b>	<b>100</b>

## **Part II: HIERARCHICAL PROCESS OF FACIAL IDNETITY.....102**

### **CHAPTER 4: CATEGORICAL OR CONTINUOUS REPRESENTATION OF FACIAL IDENTITY – BEHAVIORAL WORK.....103**

<b>4.1 Introduction.....</b>	<b>103</b>
<b>4.2 Identity classification task.....</b>	<b>105</b>
4.2.1 <i>Methods.....</i>	105
4.2.2 <i>Results &amp; Discussion.....</i>	107
<b>4.3 Similarity judgement task.....</b>	<b>108</b>
4.3.1 <i>Methods.....</i>	108
4.3.2 <i>Results &amp; Discussion.....</i>	109
<b>4.4 Identity discrimination task.....</b>	<b>111</b>
4.4.1 <i>Methods.....</i>	111
4.4.2 <i>Results &amp; Discussion.....</i>	113
<b>4.5 Perceptual discrimination Task.....</b>	<b>114</b>
4.5.1 <i>Methods.....</i>	114
4.5.2 <i>Results &amp; Discussion.....</i>	115

**CHAPTER 5: DIFFERENT TYPES OF REPRESENTATIONS IN THE BRAIN –  
AN fMRI AND PRIMING EXPERIMENTS.....118**

<b>5.1 Identity and physical representations in the brain – an fMRI experiment.....</b>	<b>118</b>
5.1.1 <i>Methods.....</i>	119
5.1.2 <i>Results &amp; Discussion.....</i>	121
<b>5.2 Gender judgement - priming experiment.....</b>	<b>126</b>
5.2.1 <i>Methods.....</i>	126
5.2.2 <i>Results &amp; Discussion.....</i>	127
<b>5.3 Familiarity judgement - priming experiment.....</b>	<b>129</b>
5.3.1 <i>Methods.....</i>	129
5.3.2 <i>Results &amp; Discussion.....</i>	130
<b>5.4 Effects of pre-experimental familiarity.....</b>	<b>132</b>
5.4.1 <i>Perceptual modulation by pre-experimental familiarity....</i>	133
5.4.2 <i>Extent of familiarity modulates brain sensitivity to             changes in faces.....</i>	134
5.4.3 <i>Familiarity modulation of facilitation priming effects.....</i>	135
<b>5.5 General discussion.....</b>	<b>136</b>

**Part III: EARLY FACE PROCESSES.....138**

**CHAPTER 6: PROCESSING SPATIAL INFORMATION FROM A FACE...140**

<b>6.1 Introduction.....</b>	<b>140</b>
6.1.1 <i>Two sub-cortical pathways.....</i>	140
6.1.2 <i>Coarse-to-fine or flexible usage hypothesis.....</i>	142
6.1.3 <i>SF information and processes of identity.....</i>	143
6.1.4 <i>Computational models.....</i>	144
6.1.5 <i>Neuroimaging studies.....</i>	144



6.2 Methods.....	146
6.3 Results.....	150
6.4 Discussion.....	155
 <b>CHAPTER 7: PROCESSING FEATURAL AND CONFIGURAL INFORMATION FROM A FACE.....</b>	 <b>159</b>
7.1 Introduction.....	159
7.1.1 <i>Defining features and configuration</i> .....	159
7.1.2 <i>The Configuration approach for face processing</i> .....	160
7.1.2a Cognitive research.....	160
7.1.2b Neuropsychological research.....	161
7.1.2c Human as face experts.....	162
7.1.3 <i>Electrophysiology recording in monkeys</i> .....	164
7.1.4 <i>Neuroimaging studies in human</i> .....	165
7.2 Identity discrimination experiment – behaviour work.....	167
7.2.1 <i>Methods</i> .....	167
7.2.2 <i>Results &amp; Discussion</i> .....	168
7.3 Pair repetition paradigm – an fMRI study.....	174
7.3.1 <i>Methods</i> .....	174
7.3.2 <i>Results &amp; Discussion</i> .....	175
7.4 The role of featural and 2 <sup>nd</sup> -conf information in face recognition..	181
7.4.1 <i>Methods</i> .....	182
7.4.2 <i>Results &amp; Discussion</i> .....	185
7.5 Summary.....	188
 <b>Part IV: Processing variant aspects of a face: the case of expression.....</b>	 <b>190</b>
 <b>CHAPTER 8: FEAR BIAS EFFECTS ON NEURONAL RESPONSES TO EXPRESSIONS.....</b>	 <b>194</b>
8.1 Methods.....	194
8.1.1 <i>Hexogen expression task</i> .....	194
8.1.2 <i>fMRI and EEG experiments</i> .....	196

<b>8.2 Results.....</b>	<b>198</b>
8.2.1 <i>Hexogen expression task.....</i>	198
8.2.2 <i>One back task, imaging experiments behavioural results... </i>	199
8.2.3 <i>EEG experiment.....</i>	200
8.2.4 <i>fMRI experiment.....</i>	204
<b>8.3 Discussion.....</b>	<b>208</b>
 <b>CHAPTER 9: AMYGDALA ROLE IN EARLY EXPRESSION</b>	
PROCESSING.....	211
<b>9.1 Methods.....</b>	<b>211</b>
<b>9.2 Results.....</b>	<b>213</b>
9.2.1 <i>Hexogen expression task.....</i>	213
9.2.2 <i>One-back task.....</i>	219
9.2.3 <i>EEG experiment.....</i>	220
9.2.4 <i>fMRI results.....</i>	226
<b>9.3 Discussion.....</b>	<b>232</b>
 <b>Chapter 10: GENERAL CONCLUSIONS.....</b>	
10.1 Hierarchical structure of face processing.....	238
10.2 What constitutes early face processing.....	241
10.3 Early processing of facial expressions.....	243
 <b>LIST OF FIGURES.....</b>	<b>246</b>
<b>LIST OF TABLES.....</b>	<b>249</b>
<b>REFERENCES.....</b>	<b>250</b>

# PART I:

## INTRODUCTION

---

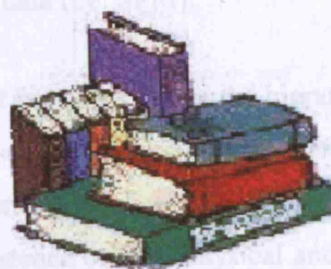
# LITERATURE REVIEW AND METHODOLOGICAL BACKGROUND

### 1.1. THESIS OVERVIEW

This thesis is divided into four parts. In the first part (Chapter 1) I review three models of face processing and cognition (Bruce and Young, 1986) and two methodological approaches (Friston et al., 1994; Friston, 2000). These hypotheses are drawn from these models, the first relates to the hierarchical nature of face processing, the second concerns the dissociation of familiar and unfamiliar faces and the third relates to the dissociation of identity and expression processing. The literature review focuses on these hypotheses.

The method chapters (Chapters 2 and 3) describe the basics of magnetic resonance imaging (MRI) and of electroencephalogram (EEG) and the underlying assumptions regarding the sources of these data and how to analyze the data (SPM).

Part II describes the identity and expertise and focuses on the dissociation of identity and expertise. Here, I start by providing evidence for the dissociation of identity and expertise processing. I then show that these two processes are dissociated in the hierarchical processing of face information. The chapter concludes by demonstrating familiarity effects on categorization of face identities.



SPM



# CHAPTER 1:

## INTRODUCTION

---

### 1.1 THESIS OVERVIEW

This thesis is divided into four parts. In the first part (**Chapter 1**) I review three models of face processing, one cognitive (Bruce and Young, 1986) and two neuroanatomical models (de Renzi et al., 1991; Haxby et al., 2000). Three hypotheses are drawn from these models, the first relates to the hierarchical nature of face processing, the second concerns the dissociation of familiar and unfamiliar faces and the third relates to the dissociation of identity and expression processing. The literature review focuses on these hypotheses.

The method chapters (**Chapters 2 and 3**) describe the basics of magnetic resonance imaging (MRI) and of electroencephalogram imaging (EEG), the underlying assumptions regarding the sources of these data and the tools used here to analyze the data (i.e. SPM).

Part two aims to test the hierarchical nature of face identity processes and focuses on dissociating physical and identity processing. Here, I used a morphing technique to quantify physical changes in a face. I start by providing behavioural evidence for existence of both physical and identity processing (**Chapter 4**). Then, using fMRI, I show that these two processes are anatomically dissociated and correspond to hierarchical anatomical axis (**Chapter 5**). Two additional priming experiments provide further evidence for differential involvement of physical and identity processes that depended on the task. The chapter concludes by demonstrating familiarity effects on categorization of face identities.

Part three focuses on early face processing of physical information. Physical information from a face was defined in two ways: first, as the physical nature of the visual input (i.e. spatial frequencies; **Chapter 6**) and second as the cognitive components of a face (i.e. feature and configuration; **Chapter 7**). I demonstrated that in posterior occipital cortices different types of information from a face are processed separately. In a follow up behaviour experiments, I demonstrated that while featural information is more important to individuate faces, configural information is more important for face recognition.

Part four deals with the processing of expressions. Combining fMRI, EEG and behaviour, I demonstrated an early ERP differential response to facial expression (110 – 200msec) that was modulated by subject perception (i.e. tendencies to ‘read’ fear expression in a face; **Chapter 8**). The anatomical origin of the early ERP expression effect was tested with epileptic patients that either had a lesion or an intact amygdala (**Chapter 9**). It was demonstrated that a lesion to the amygdala influenced an early ERP expression differential response. More specifically a lesion to the amygdala disrupts the early ERP expression effect during fear perception. Dissociation between automatic fear responses mediated via the amygdala, and expression perception that is mediated via occipital-temporal regions, is proposed. The thesis concludes by revisiting the three hypotheses drawn in the introduction, in light of the new results.

## 1.2 A FRAMEWORK FOR UNDERSTANDING FACE PERCEPTION

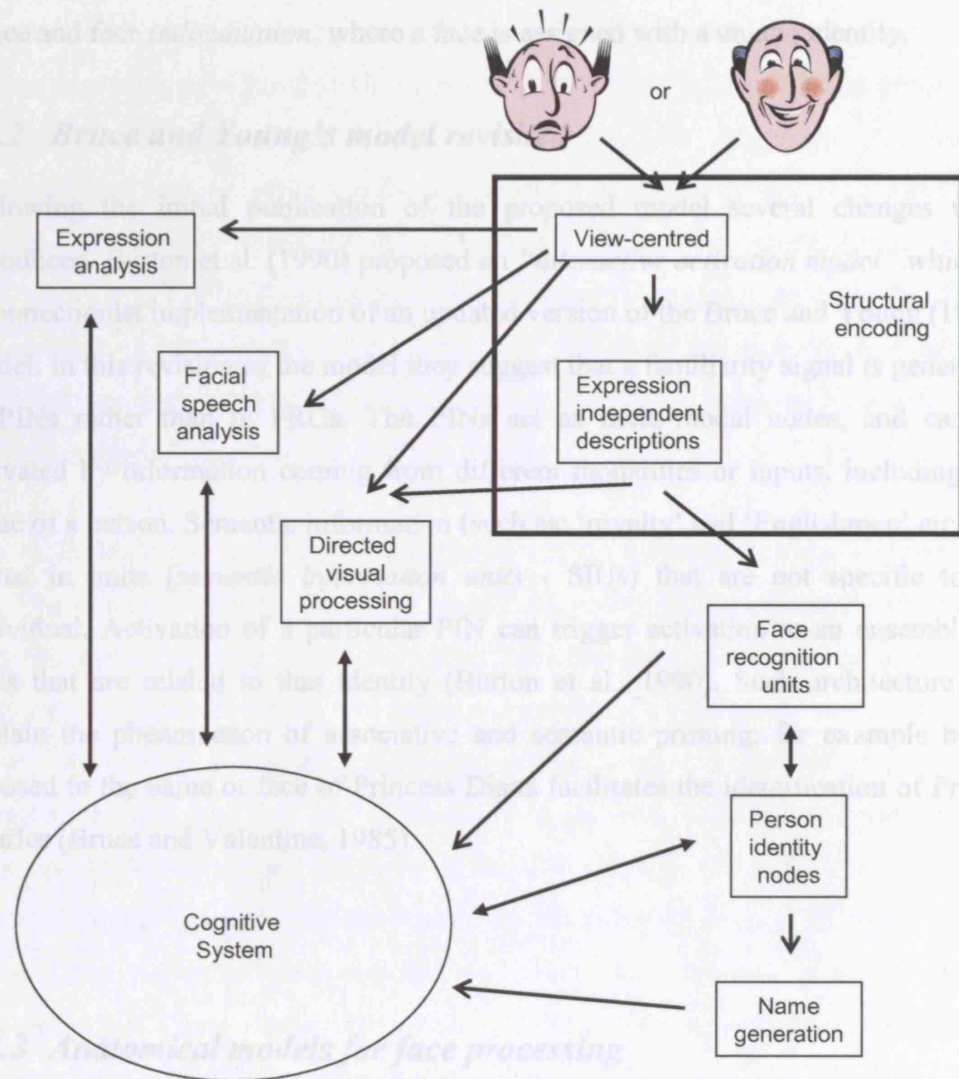
### 1.2.1 *Bruce and Young's (1986) face recognition model*

The dominant framework for understanding face processing remains that of Bruce and Young (1986). This model suggests that faces are processed in parallel pathways that each extracts different properties of a face; such as identity, expression, speech etc. The authors distinguish between processes engaged by all faces (structure encoding, expression, speech etc.) and processes engaged when previously known faces are encountered. According to the model (**Fig. 1.1**) the initial phase in face processing is a *structural encoding phase*. This phase encompasses two steps. The first encodes a viewed-centred description of a face at a given moment, and enables detailed description, such as specific lightening conditions, shape of the features, head position etc. In a natural environment this representation is constantly changing and updated depending on the visual input. The initial encoding generates a *view-centred* representation of a face, and following this initial encoding, several different processing streams diverge, including pathways for encoding facial expressions, extracting speech related cues and a third pathway for processing identity.

The face identity pathway is the prime focus of the model. Here, within the *structural encoding phase* a second step ensues that involves extracting an abstract representation of a face. This representation is independent of viewing conditions and facial expression and is used for comparisons with stored codes of familiar faces, termed a *face recognition unit* (FRU). Bruce and Young (1986) argue that familiar (i.e. a previously known person) and unfamiliar faces are processed from this stage onward in separate pathways. While a familiar face will activate an FRU that contain abstract visual code of it, unfamiliar faces will engage short term memory processes that are not specified in the model and are referred to as *directed visual processing*. This highlights one major limitation of the model that it does not explain how an unfamiliar face becomes familiar (Bruce et al., 1992).

*Face recognition units* (FRUs) are structural codes that provide descriptors for a previously known face. A familiarity signal for a known face is generated if there is a match between the representation encoded in the structural encoding phase and an FRU – leading to recognition. The strength of this familiarity signal depends on the level of similarity between the two codes. There is one FRU for each known person.

Familiarity signals generated by an FRU may trigger activation in a corresponding *person identity node* (PIN), which generate a more elaborate identification of a face. PINs are part of an associative memory network and contain stored semantic information regarding a particular individual. There is one PIN for each known individual. PINs as opposed to the FRUs, can be triggered by information from non-visual modalities, such as a person's voice, his or her name etc. The FRUs can be activated or put on standby by a PIN (for example when expecting to meet someone). This suggests that FRU can be modulated by a top down process; though note that FRUs contain only visual information. It is not clear from the model whether PINs store visual information related to the person's face or semantic knowledge alone. A person's name is a symbolic representation of a particular person and has a unique structure in the model (Bruce and Young, 1986, **Fig. 1.1**). Note that this model hypothesises a categorical representation of the FRUs and PINs, i.e. one unit for each identity as opposed to a continuous nature of representation in the *structural encoding* phase, this hypothesis will be tested in **Part II**.



**Figure 1.1:** Face recognition model adapted from Bruce and Young 1986.

Face perception is described to have a hierarchical structure with several parallel branches that diverge after an initial view-centred phase, one for expression, one for speech processing, one general and a fourth for identity of familiar faces.

In line with this proposed model, I will use the term *perception* to describe early face processing stages, possibly related to the structural encoding phase. I will use *recognition* to describe the generation of a familiarity signal that can be dissociated from any semantic, associative and contextual information about a face. Finally, *identification* I take to reflect processes involved in retrieving semantic and contextual information that might include the name of a viewed face. Two additional early stages of face processing that are not specified in the model but would be



referred to in this thesis are: face *detection*, whereby a visual object is categorized as a face and face *individuation*, where a face is assigned with a unique identity.

### ***1.2.2 Bruce and Young's model revisited***

Following the initial publication of the proposed model several changes were introduced. Burton et al. (1990) proposed an “*interactive activation model*” which is a connectionist implementation of an updated version of the Bruce and Young (1986) model. In this revision of the model they suggest that a familiarity signal is generated in PINs rather than in FRUs. The PINs act as multi-modal nodes, and can be activated by information coming from different modalities or inputs, including the name of a person. Semantic information (such as: ‘royalty’ and ‘Englishmen’ etc) are stored in units (*semantic information units* - SIUs) that are not specific to an individual. Activation of a particular PIN can trigger activation in an ensemble of SIUs that are related to that identity (Burton et al., 1990). Such architecture can explain the phenomenon of associative and semantic priming; for example being exposed to the name or face of Princess Diana facilitates the identification of Prince Charles (Bruce and Valentine, 1985).

### ***1.2.3 Anatomical models for face processing***

#### **1.2.3a Neuropsychological model**

Prosopagnosia is a condition that is defined as impaired recognition of previously familiar faces, which in severe cases might include failure to recognize one's own face in the mirror (Bauer, 1986). This condition can be dissociated from other face perceptual impairment (Benton and Van Allen, 1972) and has inspired extensive research into the mechanisms of face recognition. Prosopagnosia can be either acquired or congenital.

Inspired by the Bruce and Young face recognition model (1986) several suggestions have been made to sub-divide prosopagnosia related phenomena (de Renzi et al., 1991; Sergent and Signoret, 1992; Young 1992). De Renzi et al. (1991) argued that prosopagnosia is a special case of object agnosia. Therefore it can be dissociated into

distinct types: perceptual (i.e. apperceptive) and semantic (i.e. associative), as suggested by Lissauer (1890) for object agnosia. Apperceptive prosopagnosia can be characterized as impairment in face perception measured by identity matching tasks and non-identity face perceptual tasks, such as gender judgement. Associative prosopagnosia on the other hand, is characterized by an absence of perceptual deficits but with face related semantic memory deficits. It is important to note, that de Renzi et al.'s (1991) proposal for subdivisions only applies to patients who fail to recognize familiar faces (Benton, 1990), and that there are patients who are not diagnosed as prosopagnosic but nevertheless have an impaired perception of unfamiliar faces (Benton and Van Allen, 1972).

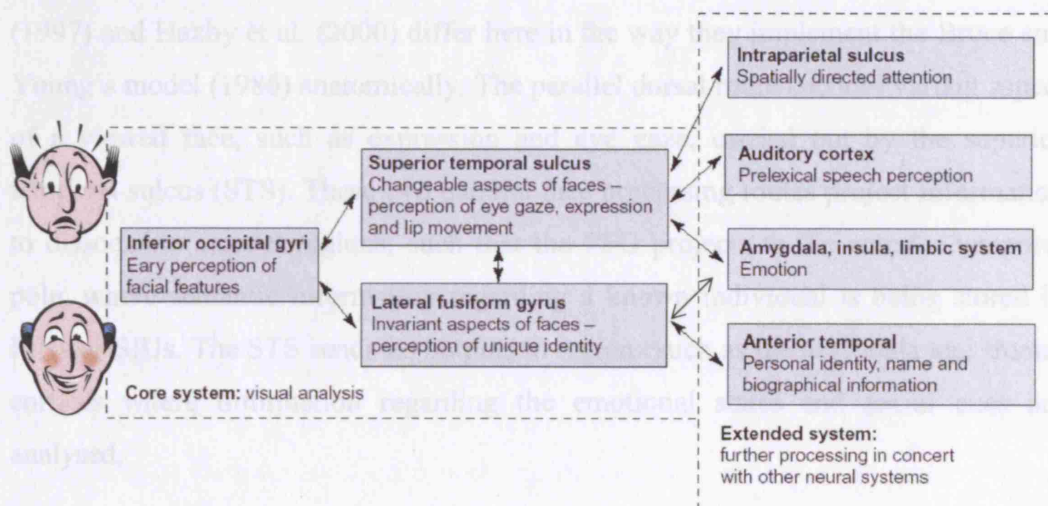
The subdivision proposed by de Renzi et al. (1991) broadly conforms to the Bruce and Young model (1986). The latter posit that prosopagnosia conditions can result from breakdown at different stages within the hierarchical process of facial identity (Sergent and Signoret, 1992). For instance, damage at a putative structural encoding phase, particularly in its later view-independent stage would involve perceptual impairment measured by face perceptual tasks and would correspond to an apperceptive prosopagnosia (de Renzi et al., 1991; Young, 1992). On the other hand deficits of the FRUs will lead to failure to elicit a familiarity signal for the sight of a known face (failure of recognition), but would be associated with intact face perception. (de Renzi et al., 1991; Young, 1992). A breakdown in the connection between FRUs and PINs would result in failure to extract semantic information that relates to a known face such as a failure in identification that corresponds to associative prosopagnosia (de Renzi et al., 1991; Young, 1992). However as opposed to Bruce and Young (1986), de Renzi et al. (1991) argue that face identity processing is not a strictly forward hierarchical model and apperceptive and associative processes operate simultaneously and facilitate each other.

De Renzi et al. (1991) also proposed a neuroanatomical model for prosopagnosia, postulating that lesions to the posterior occipital cortex result in apperceptive prosopagnosia. Lesions to more anterior regions, specifically to the anterior temporal pole lead to associative prosopagnosia with intact perception of faces but impaired recognition and identification of familiar faces (de Renzi et al., 1991). A more detailed anatomical model was proposed by Sergent and Signoret (1992), whereby

the right lingual or the posterior fusiform gyrus are suggested as involved in *structural encoding* of familiar and unfamiliar faces; while the anterior temporal cortices are suggested as involved in storing visual and semantic information about previously known individuals.

### 1.2.3b Distributed neural network of face processing

Haxby and colleagues (2000, 2002), along similar lines to de Renzi et al. (1991) and Sergent and Signoret (1992), have recently proposed a functional neuroanatomical account to face processing. Using a similar psychological architecture to the Bruce and Young model, they have argued for a hierarchical system that is divided into two parallel pathways (Fig. 1.2).



**Figure 1.2:** Distributed neural network for face processing adapted from Haxby et al., 2002. Face perception is described to have a hierarchical structure with two parallel branches that diverge after an initial stage, one for variant aspect of a face such as expression and speech and for invariant aspect of a face such as identity. The model is divided to two systems: a core system for analysing visual information from a face and an extended system which is a-modal and is not restricted to processing of visual information.

Here, the initial face processes are instantiated in the posterior occipital cortex specifically in the inferior occipital gyrus (IOG). The model does not specify the exact role of the IOG, but postulates that due to its anatomical location (i.e. posterior occipital) it is likely to be involved in early processing of facial features. An aim of the current thesis is to describe and define in more detail the nature of these early

face processes with respect to their implementation in posterior occipital cortices **(Part III)**.

Similar, to the Bruce and Young (1986) model, after an initial processing stage, output from the IOG is fed forward along two parallel pathways; these constitute a ventral pathway for processing invariant aspects of a face and a dorsal pathway for processing variant aspects of a face. In the ventral pathway, information is projected from the IOG to the fusiform gyrus (FFG) where invariant aspects of a face are encoded to extract identity information. In terms of the Bruce and Young model (1986), coding of invariant aspects of a face occur either in the view-independent representation in the *structural encoding* phase (Kanwisher et al., 1997) or the anatomical homologues of the FRUs (Haxby et al., 2000). Note that Kanwisher et al. (1997) and Haxby et al. (2000) differ here in the way they implement the Bruce and Young's model (1986) anatomically. The parallel dorsal route encodes variant aspect of a viewed face, such as expression and eye gaze, carried out by the superior temporal sulcus (STS). These two parallel face processing routes project information to dissociable amodal regions, such that the FFG projects to the anterior temporal pole, where semantic information regarding a known individual is being stored in PINs or SIUs. The STS sends its outputs to regions such as the amygdala and frontal cortices where information regarding the emotional states and social cues are analysed.

Alternative views dissociate between face detection and face recognition processes. Thus, face detection processes are postulated to occur in the posterior occipital face area (OFA) (de Gelder and Rouw, 2001) or involve sub-cortical pathways, specifically the magno-cellular visual pathways (Morton and Johnson 1991), while face recognition processes operate in parallel and involve the FFG (de Gelder and Rouw, 2001) or other cortical regions (Morton and Johnson 1991). These models are based on findings from developmental and lesion studies. Involvement of a magno-cellular sub-cortical pathway is suggested by findings that babies prefer faces when presented in the peripheral visual field where magno cells predominate rather than in the centre of the field (Morton and Johnson 1991; Johnson et al., 1991). In the current thesis evidence for a sub-cortical route for face processing was tested by comparing brain responses to faces (fMRI and EEG) of patients with an intact

amygdala to patients with a lesion to the amygdala (**Chapter 9**). Evidence for a parallel route for face detection and recognition is suggested based on the observation that most prosopagnosia patients have intact ability to discriminate faces from other objects, though they are impaired in recognizing them (de Gelder and Rouw, 2000).

#### ***1.2.4 Functional & Anatomical predictions based on the above models***

Several clear predictions can be drawn from these models regarding face processes: **The hierarchical architecture of face processing:** Bruce and Young (1986) and Haxby et al., (2002) divide face processing into a few stages that follow one another: early face processing encompasses structural encoding followed by processing of invariant aspects of a face. In the case of a familiar face, activation of FRUs precedes retrieval of semantic information about the face, with PINs or SIUs. Haxby et al. (2000) and de Renzi et al. (1991) suggest that this hierarchical structure is implemented along ventral occipital-temporal cortices. Anatomical evidence for the hierarchical structure of face identity processing will be tested in **Part II & III**.

The flow of information and possible connections between different cognitive components in the Bruce and Young (1986) model are specified as arrows (**Fig. 1.1**). Face recognition is strictly a forward hierarchical model. For example, there is no influence of top-down input on processing in the structural encoding phase. Furthermore, face recognition cannot occur without prior face perception and face identification cannot occur without prior face recognition. Reciprocal connections occur only within the highest components of the system (**Fig 1.1**, Bruce and Young, 1986), such as between FRUs and PINs, or between the cognitive system and facial expression analysis pathway. There are also no connections specified between different parallel pathways e.g. expression and identity processes.

In contrast, Haxby et al. (2002) describe reciprocal connections between all components of the core system that process information from a face such as the IOG (early processing), STS (i.e. variant, expression) and FFG (i.e. invariant, identity). The connections are limited, though, between the core system and the extended system. The amodal components (**Fig. 1.2**) such as the amygdala cannot directly

influence activation in the IOG and can only do so indirectly via STS or FFG. De Renzi et al. (1991) suggest that associative information about a face can be obtained even with impaired perceptual processes such as in the case of apperceptive prosopagnosia. Furthermore they argue that the network is dynamic where apperceptive and associative processes constantly interact and facilitate each other (de Renzi et al., 1991).

**Early face processes:** Processes in the first stage of the structural encoding phase, possibly carried out by regions within posterior occipital cortices are sensitive to the physical properties of a face and represent a face in a view-centred format. Thus, they should be unaffected by face identity and, based on the Bruce and Young model (1986), are not susceptible to top-down modulation such as face familiarity, task demands, attention etc. Based on Haxby et al. (2002) this early face processing should occur in the IOG. These hypotheses will be tested in **Parts II & III**.

**Processes of familiar and unfamiliar faces.** Based on Bruce and Young's model (1986), familiar and unfamiliar identities are coded in different systems. Initially, structural information is extracted from both familiar and unfamiliar faces and includes view-dependent and view-independent (i.e. abstract) representations. The abstract representation is compared with stored face structural codes - FRUs. In case of a match, a familiarity signal indicating positive recognition is generated, though in case of a non-match (when a face is unfamiliar) the model does not state clearly how, and if at all, a new code is generated. The hypothesis that unfamiliar and familiar face recognition is based on dissociated systems will be tested in **Chapter 7**.

Haxby et al. (2000) do not make a distinction between familiar and unfamiliar representation of a face. Although they suggest that the FFG is the anatomical homologue of the FRUs (Haxby et al., 2000). Another possibility is that the FFG is the anatomical site where initial view-independent structural codes of all face identity is generated (Kanwisher et al., 1997). Thus, it is predicted that it responds to both familiar and unfamiliar faces. The role of the FFG in identity representation will be tested in **Chapter 5**.

**The nature of visual information that is stored in the FRUs.** If the FRUs store codes that are independent of viewing conditions, reflect previously known individuals and there is one FRU per individual, then its activation should neither be generated nor modulated by non-identity attributes of a face, such as age, expression, or any change in viewing conditions. More so its activation should be categorical, with one response to all possible views of a particular identity. This hypothesis will be tested in **part II & III**.

**Different information from a face,** the various models state that identity, expression and gender are processed in dissociable and independent routes. This implies, for instance, that processing facial expression does not affect processing of facial identity. Moreover, as all face processing is initiated in posterior occipital regions, it would be predicted that a dissociation of expression and identity processing would be observed only between later stages, such as between the FFG (identity), the STS (expression analysis) and the amygdala (expression, emotion). Similarly, temporal dissociation between expression and identity processing should be observed after an initial stage of face processing. This hypothesis will be tested in **Part IV**.

## **1.3 COGNITIVE PSYCHOLOGY RESEARCH**

### ***1.3.1 Evidence for hierarchical structure***

The most intuitive example of the hierarchical nature of face processing is the experience of a sense of familiarity toward a face coupled with an inability to retrieve the relevant semantic and contextual information regarding that person. This is assumed to reflect a blockage in connections between the FRUs, PINs and SIUs (Bruce and Young, 1986; Burton et al., 1991).

In a laboratory setting several paradigms have been applied to demonstrate this hierarchical architecture. One example is the priming paradigm (I will use the priming paradigm in two behavioural experiments in **Chapter 5**). In this paradigm

response facilitation to a target is measured in relation to pre-exposure to a prime stimulus. Facilitation is assumed to reflect overlapping processes for prime and target. If prime and target are identical images of a face then facilitation is observed for fame decision (Ellis et al., 1987; 1990) and to a lesser extent for gender judgement (Goshen-Gottstein and Ganel, 2000), suggesting that both prime and target engage fully overlapping processes. But if the prime and the target are different images of the same identity, then facilitation effects are attenuated (Ellis et al., 1987). This is taken as evidence that overlap of processes between the prime and the target are reduced and includes only stages where face representation is independent of view. Similarly, there is no facilitation of fame decision for target faces when the primes are names (Ellis et al., 1987) suggesting that semantic information, specifically a name, cannot directly trigger a corresponding FRU. Others have shown by using associative or semantic priming that identification (not recognition as above) of a famous face is facilitated if it is preceded by a related face or a name but not if it is preceded by a non-related face (Brennen and Bruce, 1991). The suggestion here is that facilitation in performance is due to overlaps in SIUs representations.

Some evidence suggests that visual information is stored in the PINs (and the SIUs). A dissociation between mental imagery and pictorial representation, such that mental images as primes facilitate more responses to targets if they are mental images as well, and vice-versa, pictures as primes facilitate responses to target pictures as opposed to mental images. This was shown for both fame decision and mental imagery tasks (Cabeza et al., 1997).

### ***1.3.2 Dissociation of familiar and unfamiliar faces***

People are excellent at identifying familiar faces even from low quality images. In contrast, under similar circumstances, recognition of unfamiliar faces is dramatically impaired, as well as performances on simple perception matching tasks (Hancock et al., 2000). Matching of unfamiliar faces is also poor across different image formats (Burton et al., 2001). The authors suggest that coding of unfamiliar faces relies mainly on pictorial cues, rather than on an invariant structural abstract representation of a face, as is the case for familiar faces. However, It could be argued that these



differences do not necessary reflect qualitative differences but rather a quantitative one, as a single exposure generates poorer structural code than one that is generated after repeated exposures to the same face in different contexts.

### ***1.3.3 Are expression and identity process in parallel?***

Facial expression judgements are not facilitated by prior exposure to a specific identity in a repetition priming paradigm, suggesting that these two processes are independent (Ellis et al., 1987). However, face identity processing interferes with an expression judgement task and identity judgement is much less affected by facial expression (Ganel and Goshen-Gottstein, 2004). In a similar manner it has been demonstrated in women that categorization of fear expression was correlated with performances on identity tasks (Campbell et al., 2002). These findings suggest that identity and expression are not processed independently as originally proposed by Bruce and Young (1986), and potential connections may exist between these two processing pathways as proposed by Haxby et al. (2000).

## **1.4 NEUROPSYCHOLOGICAL RESEARCH**

The neuropsychological literature had an important and crucial impact on the development of face processing theories. Here, I start with a brief description of the development of the face processing research. Next I present a quantitative summary of the reported findings in light of the hypothesis specified above.

### ***1.4.1 Prosopagnosia - historical background***

The first recorded case of a patient who was unable to recognize individuals by their faces, but could do so on the basis of their voices was reported in 1844 by Wigan (Sala and Young 2003). In 1867, Quaglino and Borelli reported the case of Mr. LL who was diagnosed as having impaired face perception that could not be explained as a general deficit in visual processes (Quaglino and Borelli, 1867 in Sala and Young, 2003). Quaglino in his report touched upon some of the major topics in face perception that still occupy researchers within the neuropsychological community,

and are partly addressed in the current thesis. He argued that the case of Mr. LL speaks in favour of a localization hypothesis that relates specific functions to distinct brain regions and that perception of familiar faces can be linked to the posterior right hemisphere. Quaglino also suggested a distinction between deficits relating to low or high-order visual processes and argue that impairment in face perception can be viewed as face specific and of high order.

Several more cases of patients with impairment in face perception were subsequently reported (c.f. Wilbrand, 1892 in Solms et al., 1996). About 70 years later, in 1947, Bodamer (Bodamer, 1947) termed this condition prosopagnosia (Greek for face-not-know) and explicitly argued it should be viewed as a unique disruption in face processing that is dissociable from other visual agnosia. At the time this idea was highly criticized (Benton, 1990). However, the concept of prosopagnosia has now been fully embraced by the neuropsychological community though the debate continues around the specificity of this condition to faces (de Gelder et al., 1998). This issue of face specificity processes is not addressed in the current thesis, as different types of processes are compared within the face domain and not with respect to non-face objects.

The anatomy-function relation between face processing deficits and lesion location is demonstrated in a group study where 13 out of 116 patients with focal, unilateral lesions to various sectors of the cortex were found to be significantly impaired in identifying famous faces. The patients' lesions were all confined to the right hemisphere, but the specific location of the lesions within this hemisphere varied, with the anterior temporal pole being the most common site (>9 patients out of 13) followed by the FFG (5 patients), the inferior occipital gyrus (IOG) and the superior temporal sulcus (STS) (Tranel et al., 1997). A possible way to resolve inconsistencies in the neuropsychological literature and functional imaging literature (see below) might be to enquire more carefully into the definitions and characteristics of the prosopagnosia condition and the anatomical location of lesion, as suggested by de Renzi et al. (1991); Young (1992) and Sergent and Signoret (1992).

This heterogeneous nature of the prosopagnosia syndrome was pointed out by several researchers (de Renzi, 1986, 1991; Benton, 1990) and several subdivisions of prosopagnosic patients have been proposed, these include: 1) a division along an apperceptive – associative axis; 2) a division that subsumes the hierarchical face recognition model of Bruce and Young (1986); and 3) a division of patients based on the time of onset of their condition: acquired or congenital.

In the following section, a comparative review of the neuropsychological literature of face perception is presented focusing on the main predictions drawn in the Introduction. Patients' performances on various tasks are described and plotted depending on their lesion location. The anatomical location of the lesion was based on the authors' descriptions, and if available on structural images. I focused on lesions that included ventral occipito-temporal cortices and patients that were reported to show face related perceptual impairments. The aim of this analysis was to establish a possible association between function and anatomy, in light of the models described above. Performances were described as percentages of correct response and were not equated for chance levels that varied between labs and tasks. The reason for not equating for chance level performances was that I assumed that subjects do not tend to guess, and equating for chance might lead to a loss of sensitivity or biased interpretations.

#### ***1.4.2 Evidence for hierarchical structure***

Sergent and Signoret (1992) provide evidence for possible function – anatomical hierarchical structure in prosopagnosia phenomena. They compared performances of four prosopagnosia patients and brain responses of healthy control using identical tasks that tap into different face processing stages, e.g. identity matching (*perceptual individuation*), identity *recognition*, face *identification* etc. They concluded that posterior occipital regions are involved in perceptual individuation specifically by extracting the physiognomic invariants from a face, while FFG and anterior temporal pole regions are involved in accessing stored visual and semantic representations of a known face (Sergent and Signoret, 1992).

Young (1992) reviewed several cases from the literature whereby syndromes of impaired face processing were dissociated. He presented a patient that was impaired in face recognition but not in perceptual individuation (i.e. identity matching task) while another patient showed the opposite pattern. The latter case contradicts the hypothesis drawn from a forward hierarchical model (Bruce and Young, 1986) as this model predicts that recognition cannot be achieved if early face processing (perceptual individuation) is impaired. In similar line, McNeil and Warrington (1991) argue that perceptual deficits in face processing do not predict face recognition deficits (McNeil and Warrington, 1991; Benton and Van Allen 1972). These cases suggest that identities are not processed in strict forward hierarchical structure.

Feed forward hierarchical relations are suggested to be preserved between face recognition and identification. In Young's (1992) review of single cases, all patients that showed deficits in face recognition were also impaired in retrieving semantic information. But there was also a patient that could not identify faces but could recognise them (Young, 1992), suggesting that his impairment stemmed from a deficits to a higher structure of the hierarchical stages of face processing.

In the comparative review the hierarchical model was tested using three tasks: An identity matching task (i.e. testing for perceptual individuation), a recognition task, and two identification tasks.

***Hierarchical processing of familiar faces.*** Identifying a familiar face has been suggested to involve three successive processes: perceptual (individuation), recognition and identification (Hay and Young, 1982; Bruce and Young, 1986). Recall, individuation is the ability to assign one face to one identity; recognition is a feeling that a face is familiar and is achieved by matching its current representation to a previously stored representation of it (i.e. face recognition unit, FRU). Identification, on the other hand involves associating semantic information to a face including its name. This information is accessed via a personal identity node (PIN) and is suggested to be stored using SIUs (Hay and Yung, 1982; Bruce and Young, 1986). Classical models for face recognition argue that individuation always precedes recognition, which always precedes identification (Bruce and Young,

1986). However, several neuropsychological cases may suggest a double dissociation, such as the case of Capgras patients. These patients show normal face identification but without a reliable sense of familiarity, i.e. recognition (Ellis and Young, 1990; Ellis and Lewis, 2001).

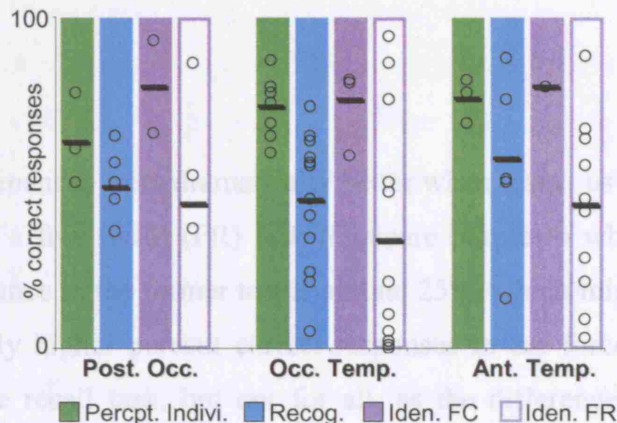
Prosopagnosic patients complain mainly about the loss of feeling of familiarity and their inability to identify well known individual by their faces. Nevertheless some prosopagnosic patients are able to recognise familiar faces that are presented in the context of a force-choice task even though they could not identify these same faces. Note, that often when comparing recognition to identification, recognition is tested using a force-choice task while identification is tested using a free recall. Thus comparing performances on recognition and identification tasks is problematic as this comparison is confounded by unrelated cognitive processes. A more comparable identification task is when identification is tested using a force-choice task as well. In such tasks the patient is given a name and required to choose the corresponding face out of four or more distracters (Barton et al., 1991).

To assess structure-function hierarchical relation for face identity processing, I divided patients based on the location of their lesion. **Figure 1.3** shows the distribution of performance on four tasks (identity matching, perceptual; force-choice recognition; force-choice identification; free recall of identity) for the three different lesion sites (posterior occipital, occipito-temporal, anterior temporal). Percentage of correct responses are presented, though note that for the force-choice tasks, chance performance can vary from 25% - 50% depending on the amount of distracters used in the different experiments.

Evidence for hierarchical structure of face processing can be seen along the posterior-anterior axis in the results for the identity matching task which test for the ability to individuate faces (**Figure 1.3**, see the green bars). Lesions to posterior occipital are associated with more severe identity perceptual deficit compared to more anterior lesions. This confirms the de Renzi et al. (1991) distinction between apperceptive and associative prosopagnosia that link posterior lesions to apperceptive type of impairments while anterior lesions do not impair individuation processes.

**Figure 1.3: Hierarchical face processing**

Distributed performances (% correct response) on four tasks: Perceptual identity matching (i.e. Individuation, green); force-choice recognition (Recog, turquoise); force-choice identification (Iden. FC, purple); free recall of face identity (Iden. FR, white). Black line represents the average of the group, circle individual patients performances. Patients reported in: Carlesimo et al. 1998; Papagno and Muggia, 1999; de Gelder and Row 2000; Braton et al. 2001; Wada and Yamamoto, 2001; Mendez and Ghajarnia, 2001; Sperber and Spinnler, 2003; Joubert et al. 2003; Mattson et al. 2003; Bobes et al. 2003; Snowden et al. 2004; Delvenne et al. 2004.



As can be seen in **figure 1.3**, patients vary in their performances across all tasks. An important thing to note is that patients were tested on variable number of stimuli hence it might have led to a bias in the percent of correct responses; for example in the case of free recall identification some patients were tested on 50 famous faces (Bobes et al., 2003) while others on only 6 (Clarke et al., 1997), more so the table includes data from temporal dementia patients (Snowden et al., 2004) which might account for the relatively high accuracies in the free recall test of patients with a temporal lesion. Nevertheless trends can be observed but should be interpreted with caution.

Focusing on the perceptual individuation task of identity matching (**Figure 1.3**, see the green bars) it can be seen that lesions to posterior occipital are associated with more severe deficits compared to more anterior lesions. This confirms the hierarchical model offered by de Renzi et al.'s (1991) distinction between apperceptive and associative prosopagnosia that link posterior lesions to apperceptive type of impairments while anterior lesions do not impair individuation processes. Furthermore, identification processes tested with FR (but not with FC) seem to be more impaired with anterior temporal lesions than with more posterior lesions. Recognition processes seem to be more impaired with lesion to occipito-temporal cortex and slightly less if the lesions affected posterior occipital or anterior temporal

cortices. This suggests that sense of familiarity to a known face might be mediated via occipito-temporal cortices.

As expected, identification performances were dramatically better when tested using a forced-choice (FC) rather than a free recall (FR) task (compare purple to white bars). Recall that chance performance in the former test is around 25%, which might account for some of the relatively higher percent correct responses in the forced-choice task compared to the free recall task, but not for all, as the difference is greater than 25%.

Intriguingly, when identification and recognition were both assessed using FC tasks, identifying a face seemed to be better than recognizing it. This difference becomes even greater when chance levels are taken into account, because in FC recognition tasks chance performances were around 50%, (familiar, unfamiliar) while in FC identification tasks chance performances varies from 25-50%. This contradicts the predictions of the hierarchical processing model in which recognition precedes identification. One possible way to resolve this puzzle is to modify the type of information that is stored in the PINs and SIUs, so as to include visual information and not just semantic. In this way accessing the PINs or activating SIUs also enables one to retrieve information about the visual appearance of a person, providing an alternative top-down route for matching visual information to a stored mental image. Support for the latter proposition comes from studies of prosopagnostic patients who can retrieve visual information about a face through imagery processes, though present inability in recognizing/identifying these faces (Young et al., 1994; Barton et al., 2003; Michelon and Biederman, 2003).

### ***1.4.3 Dissociation of familiar from unfamiliar faces***

Numerous neuropsychological studies have suggested a double dissociation between recognition of familiar and unfamiliar faces (Warrington and James, 1967; Malone et al., 1982; Takahashi et al., 1995). However, the meaning of this double dissociation

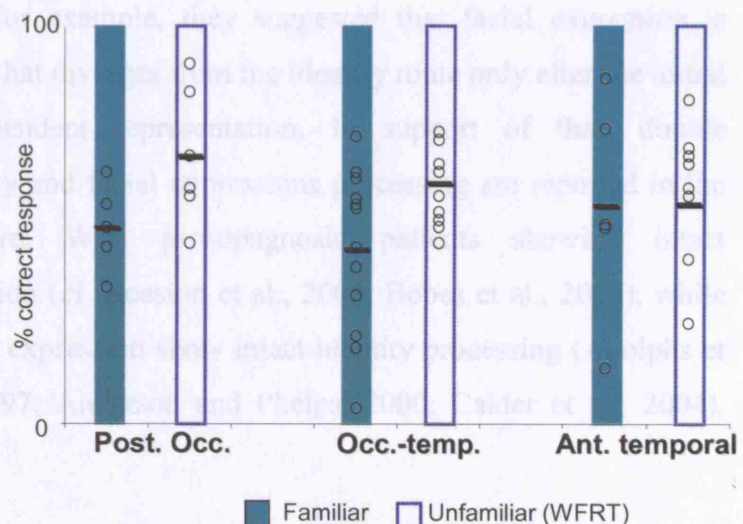


remains unclear. One possibility is that familiar and unfamiliar faces are processed via different recognition systems (Bruce and Young, 1986; Bruce and Burton, 1992). Alternatively, a more parsimonious view can describe differences between familiar and unfamiliar faces as quantitative rather than qualitative, e.g. number of exposures, variability of exposures, length of acquaintance etc. Furthermore most double dissociations observed are accounted by task demands (Goshen-Gottstein and Ganel, 2000). Tasks used to assess familiar face processing are typically associated with recognition and identification whereas unfamiliar face processing is usually assessed by perceptual tasks (e.g. Benton and Van Allen, 1972), or by short term memory tasks (e.g. Warrington and James, 1967). Therefore in the following comparative literature review I summarised results only for recognition tasks.

Recognition of familiar faces involves correct discrimination of famous/familiar faces from unfamiliar distracters. Recognition of unfamiliar faces (old/new judgement or short-delay memory encoding) is assessed using the Warrington recognition memory face test (WRMF, Warrington, 1981). The WRMF test has two phases, an encoding and a test phase. In the encoding phase patients are asked to rate the pleasantness of a face (i.e. incidental learning). In the test phase they are presented with pair of faces for which they have to choose the one they previously saw. In the WRMF the same images are used in the encoding phase and in the test phase. Standardize score show that a patient, of any age, performing below 66% of correct responses, is considered to be severely impaired (Warrington Recognition Memory Test Manual).

**Figure 1.4: Familiar and unfamiliar face recognition**

Performances in patients (% correct responses) on two forced-choice recognition tasks: familiar faces (turquoise); unfamiliar faces the "Warrington test" (white) black line averaged response of the group. Circles, individual performances. Patient detail were reported in: de Renzi, 1986; Rapcsak et al. 1996; Clarke et al. 1997; de Renzi and di





Pellegrino, 1998; Henke et al. 1998; Mendola and Corkin, 1999; Gauthier et al. 1999; Mattson et al. 2000; Wada and Yamamoto, 2001; Barton et al. 2001; 2002; Mendez and Ghajamian 2001; Sperber and Spinnler, 2003; Bobes et al. 2003; Joubert et al. 2003; Rossion et al. 2003a; Delvenne et al. 2004.

**Figure 1.4** shows the distribution of correct responses for familiar and unfamiliar faces, divided by lesion site. Intriguingly, recognition of unfamiliar faces seems to be better than recognition of familiar faces. This contradicts results in healthy volunteers, where recognition of familiar faces is superior to recognition of unfamiliar faces (Hancock et al., 2000). Recall, however that these two recognition tasks are different in many aspects. WRMF for unfamiliar faces use short-delay between study and test (in the order of minutes) hence rely on short-term memory. Furthermore the same face-image is used in the encoding and test phase and all faces are learned after the lesion was acquired. In contrast, in the familiarity recognition test there is no learning phase and the test images might be completely new to the patients and performances being based on encoding that were prior to the lesion. Thus, interpretation about these differences reflecting dissociations between familiar and unfamiliar faces should be made with caution.

Regarding the question of structure-function relation, it seems that as lesions are more anterior the performances on the Warrington tests are more impaired. Performances seem to be slightly more impaired for familiar faces in patients with lesions that include occipital-temporal cortices.

#### ***1.4.4 Dissociation of expression, age, gender from identity processes***

Bruce and Young (1986) and Haxby et al. (200) argued that different aspects of face are processed in parallel. For example, they suggested that facial expression is processed in a parallel route that diverges from the identity route only after the initial encoding of the view-dependent representation. In support of that, double dissociations between identity and facial expressions processing are reported in the neuropsychological literature. With prosopagnosic patients showing intact recognition of facial expression (cf. Rossion et al., 2003; Bobes et al., 2003), while patients with impaired facial expression show intact identity processing (Adolphs et al., 1994; Phillips et al., 1997; Anderson and Phelps, 2000; Calder et al., 2004).

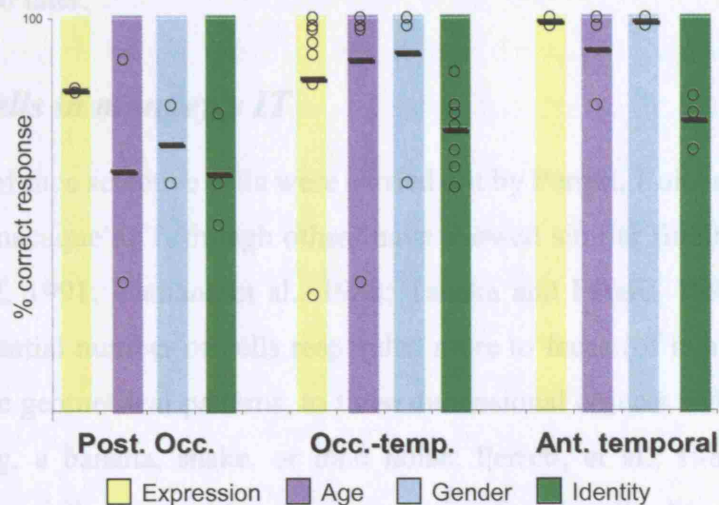
Some of these later cases are patients with lesions to the amygdala. The relation of the amygdala lesion and explicit recognition of expression is presented in more details and tested in **Part IV**.

Here, a comparative review of the literature summarise the reports of patients' performances on four different tasks that require retrieval of different types of information from an unfamiliar face: Its expression, gender, age and individuation of identity. Expression, gender and age were tested using classification tasks, while individuation of faces was tested using the standardized test for face identity perceptual deficits - the Benton face recognition test (BFRT, Benton and Van Allen 1972). In this task, patients are required to match between identities of unfamiliar faces appearing as identical images or under different viewing conditions. To test for functional dissociations and their relation to the anatomical lesions, patients were divided into three lesion groups based on the most posterior extension of their lesion site: posterior occipital, occipito-temporal and anterior temporal (**Fig. 4.1**).

**Figure 1.5** shows that occipital lesions are most commonly associated with impairment in gender, age and face individuation tasks involving unfamiliar faces. In general, as the lesions affect more anterior parts of the ventral stream performances on gender, age and face individuation tasks improve. However, note that the differences in performance on gender and age, compared with individuation of identity task increases, as the lesions are to more anterior regions. Surprisingly, processing of expressions seems to be minimally impaired following occipital lesion. This might suggest that expressions can be processed through a different route that diverges before visual information reaches the occipital cortex. These last results, however, should be treated with caution, due to the small number of patients described (e.g. 2 patients in the Occ. Expression task group).

**Figure 1.5: Face processing of identity and non-identity information**

Percent correct responses on four processes types of unfamiliar faces in patients with occipital and temporal lesions. The black line represents the averaged performances across the group. The circles represent performances of individual patients. The yellow columns represent results for facial expression tasks.



The purple columns represent results for age judgement tasks. The light blue for gender decision task and the green columns represent results for the identity matching task. Abbreviations: Post. Occ. – patients with lesions to posterior occipital cortices; Occ.-Temp. – Patients with lesions to occipito-temporal cortices; Ant.temporal – Patients with lesion to temporal and anterior temporal cortices. Data represent total of 17 patients reported in: Clarke et al. 1997; de Renzi and di Pellegrino, 1998; Henke et al. 1998; de Gelder et al. 1998, 2003; Mattson et al. 2000; Wada and Yamamoto, 2001; Bobes et al. 2003; Rossion et al. 2003; Joubert et al. 2003; Sperber and Spinnler, 2003; Delvenne et al. 2004.

In summary, the neuropsychological literature offers some anatomical support to the hierarchical organization of face processing. It also offers some support to the notion that processing different types of information from a face is implemented in parallel routes, with processing of gender, age and identity originating in posterior occipital cortices, and only identity processing are associated with processing in the ventral visual stream, with the exception of facial expression processing that seem not to be affected by lesion to posterior occipital cortices. Furthermore, there was no conclusive evidence that processing of familiar and unfamiliar faces is implemented in different anatomical regions.

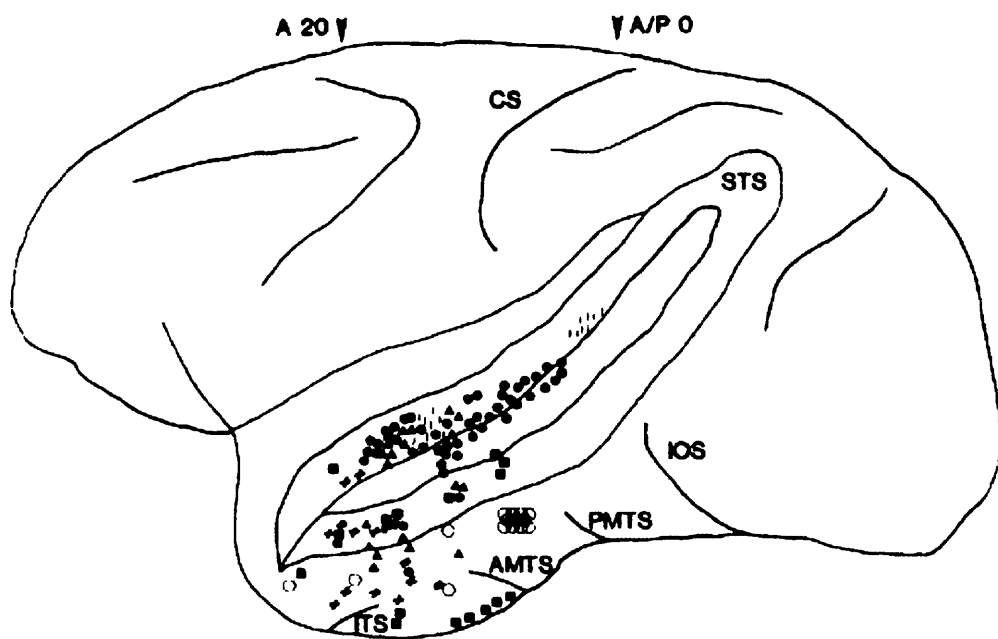
## 1.5 ELECTROPHYSIOLOGY RESEARCH IN MONKEYS

Neurophysiology studies describe several regions in monkeys' brain that contain face selective neurons. The most dense face selective neuron population was described in

the inferior temporal (IT) cortex and the superior temporal sulcus (STS), see **Figure 1.6**. Face selective neurons have also been reported in the amygdala and pre-frontal cortex and will be described later.

### ***1.5.1 Face selective cells in monkey's IT***

The most detailed studies of face selective cells were carried out by Perrett, Rolls and colleagues focusing on a macaque's IT, though others have showed similar findings (cf. Desimone et al., 1982, 1991; Yamane et al., 1988; Tanaka and Farah., 1991). Within this region a substantial number of cells responded more to faces (of human or monkeys) than to simple geometrical patterns, to three dimensional objects and to other arousing stimuli (e.g. a banana, snake, or loud noise; Perrett, et al., 1982). These neurons tend to be spatially grouped together, generating functionally discrete patches (Perrett et al., 1992). The response latency in this region is 80-160msec time-locked to stimulus onset (Perrett et al., 1984).



**Figure 1.3: Face selective cell in monkeys' brain** adapted from Perrett et al., 1992.

Location of cells in the temporal cortex selective to faces from a selection of studies projected of a cartoon of left side of rhesus macaque brain showing major sulci. Abbreviations: STS, superior temporal sulcus; IOS, inferior occipital sulcus; CS, central sulcus; ITS, inferior temporal sulcus; AMTS, PMTS, anterior and posterior medial temporal sulcus respectively. Symbols ● Perret et al., (1982, 1985, 1987); ▲ Rolls et al., (1984); ■ Yamane et al., (1988) # Hassalemo et al., (1989) | Harries et al., (1991); ○ Tanaka et al., (1991).

This apparent selectivity for faces compared to other stimuli is usually accompanied by an ability of the cell to generalize across different viewing conditions, such as different location in the visual field (Desimone et al., 1984; Tovee et al., 1994), changes in viewing distance (i.e. the face size; Rolls and Baylis, 1986), changes in direction and strength of illumination (Rolls and Baylis, 1986, Hietanen et al., 1992) and across different face orientation (upright, horizontal, inverted; Perrett et al., 1986). It should be noted that an unusual view of a face often decreased the overall magnitude and increased the latency of a face-cell response (Perrett et al., 1984).

**Encoding identity in a macaque's IT?** Some units within a macaque's IT show sensitivity to a specific identity (Perrett et al., 1984). This has raised the possibility of the existence of "grandmother cell" type organization for encoding identity (Gross, 1992; Rolls, 1992). However when considering a wide range of face identities Baylis et al. (1985) demonstrated that 77% of face selective neurons responded differently to different faces, and usually these cells have more than one preferred face. This suggests that a particular identity is represented by an ensemble of neurons and not by a single neuron (Gross, 1992). Moreover a linear increase in accuracy of identity representation as a function of the number of units recorded has been noted (Rolls et al., 1997).

### ***1.5.2 Dissociation of familiar from unfamiliar faces***

Using a repeated presentation of unfamiliar faces, up to 30% of face selective cells recorded ( $n = 22$ ) changed their response as a face becomes familiar (i.e. after its second presentation, Rolls et al., 1989). This phenomenon was not observed for repeatedly presented familiar faces. However, response alteration of cells sensitive to familiar faces can be observed when additional novel faces were added to the presented set (Rolls et al., 1989). This might suggest that cells in the IT represent face identity relative to other identities. It also suggests that the same neurons represent familiar and unfamiliar faces.

Sigala and Logothetis (2001) provide a plausible mechanism for encoding facial identity. They suggest that "face-cells" in a macaque's IT are most sensitive to the discriminative features between different faces. Using schematic faces that varied in

their features (i.e. length of nose) or second order configuration (i.e. vertical location of eyes, distance between eyes, vertical location of mouth) they generated two “identity” categories. These categories were defined based on two diagnostic attributes: the height of the eyes within a face and the distance between the eyes, while the nose length and the mouth height were non-diagnostic features. Recordings were then made from face selective cells in macaques’ IT cortex, while the monkey performed an identity categorization task. After a supervised learning session modulation of cells responses was observed for the diagnostic, but not for the non-diagnostic properties of a face. Thus, it suggests that cells encode differences between faces, and hence each unfamiliar face change the way familiar faces are encoded as well. This supports again the idea that familiar and unfamiliar faces are encoded using the same neural system, as opposed to Bruce and Young predictions (1986).

### ***1.5.3 How does the brain dissociate between expression and identity processes?***

Two ways to represent facial expression and identity can be considered. The first based on Hasselmo et al. (1989) findings suggests anatomical dissociation of identity and expression processing. Specifically, a ventral patch in the IT represents identity and a dorsal patch in the STS that represent expression. It was also demonstrated that removal of a macaque’s STS, where some face-cells are located, does not impair performance of face matching and recognition tasks, but impairs performance on gaze detection (Heywood and Cowey, 1992). This suggests that this region is also involved in gaze and expression processing, in agreement with Haxby et al.’s (2000) model.

An alternative way of encoding expression from a face was suggested by Susage and colleagues (1999). They demonstrated that expressions and identities are encoded by the response duration and amplitude of face selective neurons. Face selective cells first show a strong response to all faces and then depending on familiarity and expression maintain firing rate or attenuate it (Susage et al., 1999). Here the functional dissociation is established in the temporal rather than spatial domain.

#### ***1.5.4 Face selective cells in other regions in the monkey's brain***

Recordings from the amygdala have revealed that 4% of the cells sampled (out of a total of 1000) responded primarily to faces (Leonard et al., 1985). These cells, localized in the basal nucleus of the amygdala, show stronger responses to faces (presented 2D or 3D) when compared to simple geometrical shapes, complex 3D objects and other arousing and aversive stimuli (Leonard et al., 1985). These neurons respond differently to different individual faces, in some cases they respond to part of a face as well, and in a few cases response was stronger for a non-neutral facial expression. Face selective cells in the amygdala showed longer latencies responses (110-200msec) than the cells in the STS (90-140msec) and were more sensitive to identity (Leonard et al., 1985). Face selective cells were also observed in the ventral putamen (Rolls and William, 1987), a region that has direct connections to the IT (Gross, 1992).

Within the prefrontal cortex, face selective neurons have been identified in the inferior frontal sulcus (IFS, Pigarev et al., 1979; O'Scalaidhe et al., 1999). These neurons show face selectivity responses similar to those shown by neurons in the IT, though with a longer latency (on average 138msec). These neurons did not respond to other type of complex objects, or to other arousing, salient, or emotional stimuli, the response was unaffected by head inversion and was attenuated by a presentation of a jumbled feature face (O'Scalaidhe et al., 1999). The similarity of these cells to cells recorded in the IT is not surprising as this region receives direct input from the IT (Webster et al., 1994) and is considered to be an extension of the ventral visual stream into frontal lobe (Gross, 1992). Some face selective neurons in the IFS are sensitive to identity, others to expressions, and others to a combination of the two (O'Scalaidhe et al., 1997).

In conclusion, the preceding review suggests that within the same cortical region functional dissociations can be observed for various aspects of face properties, though different functions may be also dissociated spatially (e.g. STS versus IT) and

temporally (e.g. earlier response for a face and then for a particular identity and expression). The latter might represent a form of hierarchical processes.

## **1.6 ELECTROPHYSIOLOGY RESEARCH IN HUMANS**

### ***1.6.1 Single cell recording in humans***

Intracranial recording in humans is usually preformed as part of a pre-surgical evaluation for epileptic patients. An additional method to study the function of a region is by stimulating it - inducing a mild electrical current to excite a specific brain region and recording the patients' experiences. In both cases recording and stimulating are made from brain regions in the vicinity of a suspected epileptogenic focus and therefore are probably heavily affected by epileptic activity. Therefore data from such sources should be interpreted with caution, as it might not represent fundamental processes in the same way as in healthy intact brain.

Single cells recording in humans show face responsive cells in the ventral occipito-temporal cortex (Fried et al., 1982; Lucas et al., 2003), specifically the fusiform gyrus (Klopp et al., 1999; Mundel et al., 2003,), in the pre-frontal cortex (Marinkovic et al., 2000), the amygdala, hippocampus and entorhinal cortex (Seeck et al., 1993; Kreiman et al., 2002) and in right middle and superior banks of the temporal cortex (Ojemmann et al., 1992).

***Dissociable responses for expression and identity.*** Among visually responsive cells ~13% in the amygdala, 7% in the entorhinal cortex and 9% in the hippocampus show sensitivity to facial expressions in unfamiliar faces. Photographs of famous faces elicited a selective response in 9% of the cells in the amygdala, 5% of entorhinal cortex and 13% of hippocampus visual cells (Kreiman et al., 2002). This suggests that these regions are involved in encoding information about face expression and familiarity, though it is not clear whether or how expression and familiarity are dissociated in these regions. Some neurons have been found to respond selectively to a particular individual generalizing across viewing conditions,



pictorial cues, hair colour etc. These neurons responded also to the name of the person or to a picture where this person appeared amongst others but did not respond to physically similar looking faces, suggesting they are highly selective to a particular identity (Quiroga et al., 2005). In another study from the above group (Fried et al., 2002) single cells were recorded from similar regions during a memory task. Stimuli were either faces (8 identities with 7 different prototypical expressions including neutral) or objects. About 25% of the neurons in each region (i.e. amygdala, entorhinal cortex and hippocampus) responded to faces during the encoding phase. Some of these neurons encoded information regarding gender and expression of a face (Fried et al., 2002).

Single cell recordings from 12 humans' medial temporal cortex; revealed that 50% of recorded sites modulated their responses depending on task requirements during face perception (Lucas et al., 2003), suggesting top-down influences may affect basic face visual processing.

Electrical stimulation applied to the right fusiform gyrus (Mundel et al., 2003) impaired a patient's ability to discriminate between individual faces, suggesting a role for these regions in processing face identity. Stimulation applied to the sites that show differential EEG face effects (i.e. right FFG and inferior temporal gyrus) impaired patients' ability to name familiar faces (Allison et al., 1994).

Single-cell recordings in humans have revealed a focal region within the right ventro-lateral pre-frontal cortex of an epileptic patient that showed preferred response to faces compared to other objects (Marinkovic et al., 2000). Stimulating the same region leads the patient to report seeing a rapid succession of faces, or, when presented with a face she reported seeing it as being deformed (Vignal et al., 2000). After surgical excision of the cortex surrounding the same right prefrontal sites, the patient had a deficit in recognising expression, specifically fear, though this ability recovered after a while (Vignal et al., 2000). This last report suggests that the right pre-frontal cortex is involved in detecting faces as well as encoding their facial expression, contracting the hypothesis of completely parallel processes for expression and other face properties.

### ***1.6.2 Evoked response potentials (ERPs) of face processing***

ERP measures the averaged evoked waveform after stimulus onset (see Chapter 3 for a more detailed description of the method). ERPs can be measured on the scalp or from intracranial electrodes. Several typical face-evoked waveforms have been described in the literature.

#### **1.6.2a N170**

N170 is a negative waveform that occurs between 165-to-185msec post presentation of any visual object, with strongest negativity amplitude exhibited when subjects view humans (Botzel et al., 1989; Bentin et al., 1996; George et al., 1996) and monkey faces (Carmel and Bentin, 2001) compared to non-face objects. This waveform is larger over the right hemisphere, and is observed in lateral posterior-temporal electrodes (Bentin et al., 1996; Eimer, 1998). It is also observed as a positive component over middle-frontal electrodes (i.e. vertex positive potentials, VPP; Eimer, 1998; Rossion et al., 1999a). N170 is considered to be a face specific ERP and extensive research has been done to characterize its response to faces.

The N170 is unaffected by face familiarity (Eimer, 2000a; Bentin and Deouell, 2000, Rossion et al., 1999b; Henson et al., 2003), face repetition (Schwienberger et al., 2002; Henson et al., 2003), presentation format of a face (i.e. picture, drawing, face sketch, schematic; Sagiv and Bentin, 2001) and some suggest that it is unaffected by facial expression (Eimer and Holmes, 2002) but this is disputed by others (Sato et al., 2001; Batty and Taylor, 2003).

The N170 response is modulated by face view-angle (Eimer, 2000b), in which the strongest negative amplitude is observed for the front and profile view of the face while the cheek and back view attenuate its response, though it is still larger than for non-face objects (Eimer, 2000b). Inversion of the face delays the N170 response (Eimer, 2000c; Sagiv and Bentin, 2000) and sometimes increases its negativity amplitude (Rossion et al., 1999a). Presentation of external or internal features attenuates the N170 response, though its amplitude remains more negative than responses to non-face objects (Eimer, 2000b). It has been argued that the features that drive the N170 responses are the eyes (Bentin et al., 2001; Smith et al., 2004).

The N170 is moderately affected by task and task load requirement (Goffaux et al., 2003), though others have shown that the face-response VPP (assumed to be the anterior homologue of N170) do not differ for gender and recognition tasks (Rossion et al., 1999a). The face specific N170 response is not evident in patients with an acquired (Eimer and McCarthy, 1999) or developmental (Bentin et al., 1999) prosopagnosia. These patients showed similar response amplitude for faces and non-face objects at N170.

**Localization of the N170** - The anatomical origin of the N170 is unclear, mostly due to lack of reliable inverse solutions for localizing the scalp electric signal to particular brain structures. Hence the inconsistent results across lab localization procedures: Rossion et al. (1999) argued that the N170 for faces originates in the right inferior occipital gyrus and posterior FFG (Rossion et al., 1999); Henson and Rugg (2003) postulated that the N170 reflects activation in the STS, while others presented evidence to suggest that it reflects activation in the mid FFG (Rossion et al., 1999a; Eimer et al., 2003) or in a network of regions including the mid FFG, precunues, IOG (Mattout et al., 2005).

The N170 might reflect similar neuronal processes as recorded in occipito-temporal cortices of epileptic patients using intracranial ERP, though at a later peak 200ms (but see Bentin et al., 1996). Here, a large N200 for faces compared to non-face objects is revealed in three foci: the fusiform gyrus, inferior temporal gyrus (Allison et al., 1994) and another at the lateral bank of the occipito-temporal cortex (Allison et al., 1999). The N200 shows similar characteristic responses to the N170: responding more strongly to a whole face or eyes, it is insensitive to gaze, and is sensitive to viewing-angle with maximum response to the front-view of a face (McCarthy et al., 1999). The N200 response is attenuated for non-face stimuli even when they contain highly arousing, or aversive information. It is also not affected by face familiarity (Allison et al., 1999). These intracranial N200 suggest that the scalp recorded N170 originate from activation in the ventral and lateral occipito-temporal cortices, though the difference in the onset of the wave remains a puzzle.

**The functional role of N170** - From the accumulated empirical evidence it has been postulated that N170 reflects early face processing stages such as a *structural*

*encoding phase*; while processing of identity occurs later (see below) as hierarchical models would predict (Sagvige and Bentin, 2001; Eimer, 1999). A recent MEG study (Liu et al., 2002) suggests otherwise, as they showed that an M170 (the possible MEG homologue component of N170) is associated with identification processes rather than early face processing, as its amplitude is modulated by correct face identification but not by correct face detection (Liu et al., 2002). Note that here early face processes are defined as face detection (de Gelder and Rouw, 2001) rather than processing of a physical aspect of a face as in the Bruce and Young model (1986). In a similar vein it has been demonstrated that N170 is sensitive to perceived identity change (Camanella et al., 2000), though others argue detection of identity change occurs only at N2 (~220msec; Eimer and Mazza, 2005).

#### **1.6.2b 300 –600msec post stimuli onset**

Around 300msec after a face stimulus is presented, a dissociable response depending on face familiarity can be observed (Eimer, 2000a; Bentin and Deouell, 2000), where familiar faces elicit more positive responses compared to unfamiliar faces, a pattern that continues until about 450msec post stimulus (Eimer, 2000a; Bentin and Deouell, 2000). After this, there is a crossover where familiar faces elicit stronger negative responses than unfamiliar that last until about 650msec post stimulus (Eimer, 2000a; Henson et al., 2003). Within this time window dissociable effects of repetition priming are observed only for familiar faces (Schweinberger et al., 2002a), and the size of this effect is independent of the pictorial representation of a famous face (Schwienberger et al., 2002b). These late responses are reported to be associated with memory and retrieval processes (Henson et al., 2003).

Face selective P350 responses have also been recorded using intracranial recording, from the anterior temporal pole and STS. Responses in these electrodes show a semantic priming effect (e.g. using the name to prim the face recognition of a particular person, McCarthy et al., 1999). In terms of Bruce and Young 's (1986) cognitive model they are associated with the final stages of face processing that involve retrieving semantic information regarding a face – PIN and SIUs. Facial expressions have also been shown to elicit differential responses at that time window (Eimer and Holmes, 2002). The anatomical origin of these effects is unclear, and still

debatable, but given their length and latencies they are assumed to reflect activation within several brain foci.

### 1.6.2c P1/N1/M1

Recently studies have argued for sensitivity to faces earlier than the N170 component. Holmes and Eimer (2002) reported differential ERP responses to facial expressions already around ~135msec post stimulus onset, with fearful expressions eliciting more positive responses than neutral expressions (Eimer and Holmes 2002). This early negative component (N1) is observed over frontal electrodes. Others have found that expression modulated P1 responses (Williams et al., 2004; Pourtois et al., 2004; Meeren et al., 2005). I will present a study that aims to replicate the early expression effect in **Chapter 9**.

Liu et al. (2002) have argued for sensitivity of M1 to face detection, thus whenever subjects discriminate correctly between a face and a house, M1 amplitude increases. Similar results were observed using ERP (Itier and Taylor, 2004). This early differential response to faces versus houses will be tested in **Chapter 9**. A P1 response for faces is shown to be modulated by face repetition (i.e. 50-100msec, recorded in intracranial and scalp electrodes, Seeck et al., 1997) and by task, presumably reflecting an early attention processes (Rossion et al., 1999a).

### 1.6.2d Summary

Electrophysiology studies provide valuable temporal information of face processing. The findings above provide evidence for the hierarchical structure of face identity processes, where structural encoding precedes familiarity and identification. But they also challenge Bruce and Young (1986) and the Haxby et al. (2000) models suggesting that facial expression might be processed prior to (P1/N1) and independent of the initial structural encoding phase (N170). This hypothesis will be tested in **Part IV**.

## 1.7 NEUROIMAGING RESEARCH

Since the early nineties there have been over 400 papers published investigating the neural correlates of face perception using haemodynamic measurements (i.e. PET and fMRI). Haxby et al. (1991) was one of the earliest studies to show that a face matching task activates the ventral visual stream (i.e. occipito-temporal cortices) while a spatial matching task of non-face stimuli engages regions along the dorsal visual stream (i.e. occipito-parietal cortices; Haxby et al., 1991), though in this experiment, stimuli and tasks are confounded. Similar results for face matching tasks were obtained using fMRI (Clark et al., 1996).

### *1.7.1 Are face identity processes hierarchical?*

Sergent et al. (1992) were the first to show a posterior-anterior hierarchical structure for face processing using haemodynamic measurements (i.e. PET). They studied eight healthy volunteers during six different conditions: 1) passive viewing of a fixation cross; 2) passive viewing of unfamiliar faces; 3) gender discrimination of unfamiliar faces; 4) occupation discrimination of familiar faces; 5) living, non-living discrimination of objects; 6) grating orientation discrimination. Overlaying their PET results on a detailed structural MRI they provided the first evidence for anatomical correlates of a face processing network (Sergent and Signoret, 1992).

Gender decisions of unfamiliar faces elicit larger activation than grating orientation judgements in the right posterior occipital cortex extending to the posterior fusiform gyrus (FFG, Sergent and Signoret, 1992; Andreasen et al., 1996). Judgement of familiar face occupation elicits larger activation than judgements of unfamiliar face gender in bilateral mid FFG, right parahippocampal gyrus and bilateral anterior temporal pole. These enhanced foci of activation (apart from left FFG) are also observed when familiar faces are compared to objects (Sergent and Signoret, 1992; Andreasen et al., 1996). Activation of the posterior-anterior hierarchical axis was found when manipulating only the stimuli, whereby increased sensitivity to a whole face structure compared to scrambled faces was also observed (Clark et al., 1998;

Lerner et al., 2001). Similar hierarchical anatomical architecture was reported for the comparison of perceptual and familiarity judgement tasks that were performed on the same set of faces (Sugiura et al., 2001). Greater activation for perceptual decision tasks were observed in occipito-temporal cortices (including FFG) while familiarity judgement tasks elicited greater activation in the anterior temporal and frontal cortices (Sugiura et al., 2001). However, a recent study by Grill-Spector et al., (2004) challenge this hierarchical anatomical axis by demonstrating that detection of a face (presumably an early stage in face processing) and identification of a face, both take place within the same cortical regions (i.e. posterior occipital gyrus – and FFG, OFA and FFA respectively).

### ***1.7.2 The role of the fusiform gyrus***

As the consensus regarding the involvement of the occipito-temporal cortex in face processing emerged, Kanwisher et al. (1997) focused their research on the fusiform gyrus and introduced the term “fusiform face area - FFA”. They argued that the FFA is a module specialized in face perception. Using a surface coil over the occipital cortex in fMRI they compared responses for faces to other non-face objects. They identified several foci of activations all within the occipito-temporal cortex, from which the most reliable and consistent face region across subjects (13 out of 15) was observed in the mid fusiform gyrus. It is worth pointing out that the use of a surface coil to acquire the data limited their search volume to the occipital cortices, while excluding regions within the anterior temporal pole, or frontal cortices due to lack of signal.

Following the identification of the FFA in each subject Kanwisher et al. (1997) tested its sensitivity for other stimuli manipulations: such as comparing faces to scrambled faces, to houses and to hands. They also tested the effect of the task by comparing passive viewing to a one-back task performed on faces and hands. In all of these cases FFA showed a stronger response to faces compared to all other tested objects independent of task demands. This has been taken as evidence that the FFA is a module of face processing. An alternative view suggests that FFA is involved in subordinate discrimination. This view was rejected by Kanwisher et al. (1997) as they show that faces elicited a larger response than hands, even though for both these

stimuli a subordinate discrimination was needed to perform the one-back task (Kanwisher et al. 1997). The face module role assigned to FFA is constantly being challenged by others (sf. Gauthier et al., 2000) and I will describe this alternative view in more detail later.

FFA is suggested to be part of the early stage of face processing, similar to the N170 component, and thought to be involved in face detection and structural encoding of a face (Kanwisher et al., 1997; Rossion et al., 2003; Grill-Spector et al., 2004). In support of this it has been shown that regions within the mid FFG are sensitive to perception of faces compared to non-face stimuli when an identical set of stimuli is used and only the perception differs between conditions (Dolan et al., 1997, Hasson et al., 2001). The relation between face perception and FFG activation was also demonstrated by modulation of mid FFG response to faces by attention (Vuilleumier et al., 2001; Wojciulik et al., 1998). But the FFA has also been shown to be sensitive to face identification (Grill-Spector et al., 2004) and face familiarity (Henson et al., 2000; Rossion et al., 2003). The role of the FFA in individuation of faces rather than detecting faces per se is also evident in its sensitivity to a specific identity (George et al., 1999). Using the repetition decrease phenomenon, decreases are observed for repetition of a specific identity but not repetition of changing identity (Grill-Spector et al., 1999; Rotshtein et al., 2001; Gauthier et al., 2000; Winston et al., 2004; Eger et al., 2004). The experiment reported in **Chapter 6** touches also on this issue and where I tested the role of the FFG in identity processes.

Alternatively, it has being argued that the FFA discriminates at the subordinate-level specifically for categories that we are experts for (faces here are only an example of a category we are experts for). To support this proposition it has been shown that the FFA in an expert observer is activated when presented with their objects of expertise (e.g. Greebles, birds and cars; Gauthier et al., 1999; 2000), though other studies have failed to show such an expertise tendency of FFA, other than to faces (Grill-Spector et al., 2004).

### ***1.7.3 Involvement of other regions within occipito-temporal cortices in face identity processing***



Comparisons between faces and non-face objects usually elicit significant activation in additional regions outside the FFG, such as the inferior occipital gyrus, middle occipital gyrus, inferior temporal gyrus etc. (Kanwisher et al., 1997; McCarthy et al., 1997; Hasson et al., 2003). Ishai et al., (2002) argued for the existence of visual representations of well-known identities (triggered by visual stimuli and cued imagery) in the superior temporal sulcus and inferior occipital gyrus amongst other regions in addition to the well described FFG (Ishai et al., 2002). Despite the intense work dedicated to face processing using functional imaging, only a few studies have demonstrated dissociable roles of different regions within occipito-temporal cortex in processing information from a face (Lerner et al., 2001; Eger et al., 2004). Here I will present three studies where functional-anatomical dissociations within the occipito-temporal cortex are tested (**Chapter 6 and Part III**).

#### ***1.7.4 Representation of familiar and unfamiliar faces***

Many studies have compared brain responses for familiar and unfamiliar faces (cf. Sergent and Signoret, 1992; Gorno-Tempini et al., 1998; Phillips et al., 1998; Henson et al., 2000, 2003). I describe here only studies that have compared familiar and unfamiliar faces using identical tasks, hence avoiding task confounds. Comparisons of unfamiliar faces and familiar faces on gender decision tasks, yielded common activation in the FFG (Dubois et al., 1999) and differential activation in the amygdala and posterior occipital region showing a stronger response for unfamiliar faces compared to familiar (Dubois et al., 1999). Others have shown stronger activation for familiar faces in the FFG, and in the temporal, frontal and posterior occipital cortices (Henson et al., 2003). The last group reported increased FFG activation for familiar faces compared to unfamiliar faces using a target detection task (Henson et al., 2000), a face symmetry judgement task (Henson et al., 2003) and a fame judgement task (Henson et al., 2002). Not all studies have observed an increased response for famous more than non-famous faces in the FFG, however (Gorno-Tempini et al., 1998). Henson et al. (2000, 2002, 2003) demonstrated reduced activation for repeated presentation of famous but not for non-famous faces in the FFG. Note that in all these cases, repetition was not immediate (Henson et al., 2000, 2002, 2003). Famous as opposed to non-famous faces activated additional anterior temporal regions (Gorno-Tempini et al., 1998; Henson et al., 2003), and this

activation has been suggested to reflect retrieval of semantic and associative information (Henson et al., 2003).

Recognition of famous and newly-learned faces has been compared revealing stronger activation for famous compared to newly learned faces in the middle and anterior temporal cortex (including FFG) among other frontal, parieto-occipital and sub-cortical regions (Leveroni et al., 2000). Similar regions were observed when comparing famous to non-famous (first seen) faces in recognition tests, though here the FFG did not show a differential response (Leveroni et al., 2000). Using morph continua between newly-learned and unfamiliar faces, Rossion et al. (2001) demonstrated categorical increases in signal along the occipito-temporal cortex (in the middle occipital gyrus, FFG and the inferior temporal gyrus) for the unfamiliar compared to newly learned faces. Similarly, reduced activation for newly learned faces compared to novel faces was observed in the middle occipital gyrus and the posterior cingulate amongst other regions (Phillips et al., 1998). Note that the effect of newly-learned compared to novel or famous faces is in the opposite direction to the above studies where the familiar famous faces elicited stronger responses than the unfamiliar ones. It might be that FFG response is critically dependent on short-term exposure to a face, showing a weaker response to a newly-learned face (i.e. freshly seen) compared to famous, or non-famous distracters (Leveroni et al., 2000, Wiser et al., 2000; Rossion et al., 2001).

To summarize, findings from neuroimaging do not support Bruce and Young (1986) in their hypothesis that familiar and unfamiliar faces are processed in separate systems. Although there are differences in brain responses to familiar and unfamiliar faces these are quantitative differences and do not suggest dissociated neuronal systems (Rossion et al., 2001, Henson et al., 2000).

### ***1.7.5 Dissociation between expression and identity***

The research of expression processing has focused on the amygdala (Morris et al., 1996; Breiter et al., 1996; Phillips et al., 1998; Critchely et al., 2000; Winston et al., 2003), but processing of specific emotions have also been attributed to other regions (Surguladze et al., 2003; Phillips et al., 2004). The amygdala is also demonstrated to

show increased responses to novel faces versus famous faces (Dubois et al., 1999; Schwartz et al., 2003a; Leveroni et al., 2000), repeated faces (Rotshtein et al., 2001) and non-faces (Winston et al., 2004, Ishai et al., 2002). Similarly, the FFG which has been suggested to be involved in identity processing shows also a differential response to expression (Vuilleumier et al., 2001; Morris et al., 1998; Winston et al., 2003; Phillips et al., 2004). Thus these findings suggest that identity and expression processes are not strictly dissociated, as predicted by Bruce and Young model (1986).

Haxby et al. (2000) postulated that the FFG is involved in identity processing while the STS is in facial expression processing (see **Figure 1.2**). This hypothesis has been tested empirically by Winston et al. (2004), demonstrating that the FFG was primarily sensitive to identity change and the mid-STS primarily to facial expression change in a face pair (Winston et al., 2004). There have been many other regions that show an increased response to a non-neutral expression, amongst them the insula, calcarine, putamen, hippocampus, cingulate gyrus etc. (Phillips et al., 2004; Surguladze et al., 2003; Critchely et al., 2000). This suggests that the neuronal mechanism involved in expression processing is spread throughout the brain and might include several dissociated processing routes.

## 1.8 SUMMARY

Previous findings and theoretical models suggest that face identities are processed hierarchically. Hierarchy is shown along a temporal axis using ERP (cf. Eimer, 2000) and single cell recording (cf. Perret et al., 1984), along a cognitive axis using behavioural studies (cf. Bruce and Valentine 1985) and along a neuroanatomical axis using lesion studies (de Renzi et al., 1991). However, one gap that is left unexplored is the representation of physical aspects of faces, and its relation to encoding of identity. This aspect of face processing will be tested in part II.

The neuroanatomical models (de Renzi et al., 1991; Haxby et al. 2000) predict that early face processing occurs in posterior occipital regions. Neuropsychological data offer some support to the idea that lesions to posterior occipital cortices affect face

## Part I: Literature review and methodological background

perception. However, it is unclear what type of information is processed in early face processing. This will be tested in Part III.

Finally, numerous evidences from lesion and behavioural studies suggest that identity and expression are dissociated processes, though they may interact. Neuroimaging and electrophysiology studies have suggested that amygdala facilitates expression processing in visual cortices. It is debatable whether amygdala responses to expressions depend on projections from visual cortex (Pessoa, 2005) or maybe it precedes them (Dolan, 2002). This question will be addressed in part IV.

# CHAPTER 2:

## FUNCTIONAL MAGNETIC RESONANCE IMAGING

---

### 2.1 INTRODUCTION

Four experiments reported in this thesis measured brain responses using magnetic resonance imaging (MRI). This chapter first describes the principles of MRI data acquisition in general and in particular that of the functional MRI (fMRI). The description is influenced by the text book “MRI the basics” written by Hashemi and Bradley (1997). I next describe briefly the relation between the signal measured in fMRI and neuronal response; this is done in relation to a review written by Logothetis and Wandell (2004). Finally, I discuss the advantages and disadvantages in using fMRI measurements for cognitive neuroscience research.

The second part is dedicated to fMRI data analysis, here performed using SPM2 software (Wellcome Department of Imaging Neuroscience, UCL). SPM is a statistic toolbox that has been developed specifically to deal with data that has temporal and spatial dimensions. It will be described based on the ensemble of papers published in the book Human Brain Mapping 2<sup>nd</sup> edition, edited by Frackowiak et al., (2003).

## 2.2 DATA ACQUISITION: MRI

MRI is based on principles of nuclear magnetic resonance (NMR). It was first used as a spectroscopic technique to obtain microscopic chemical and physical information about molecules. This method is based on Felix Bloch and Edward Purcell's discovery of the magnetic resonance phenomena in 1946.

### 2.2.1 *Magnetic field*

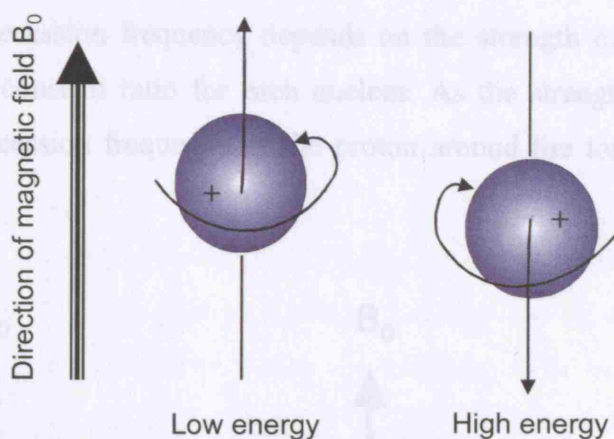
Magnetic fields can be generated by a change in electrical field, while a change in the magnetic field generates an electrical field. Together they generate an electromagnetic wave. Electromagnetic waves differ in their frequency bands. For example the x-ray electromagnetic frequency is in the range of  $1.7\text{--}3.6 \times 10^{12}$  MHz. Electromagnetic frequencies used in MRI are within the range of radio frequencies (i.e. AM, FM) 3-100 MHz. As MRI uses electromagnetic waves in the range of radio frequencies, the first step is to establish a “cleaned” controlled magnetic field environment (e.g. to avoid interference from radio waves).

The external magnetic field in MRI is used to control the initial state of the net magnetic field; this state is termed the equilibrium state. The strength of this magnetic field is in the order of 0.5–3 Tesla (T). For a comparison, the magnet used to pick up cars in junk yards is about 1.5-2.0T; the earth magnetic field is  $0.5 \times 10^{-4}$  T. In the current thesis I have used a 1.5T whole body Sonata scanner (for experiments described in **Part III & IV**) and a 3T head only Alegra Siemens scanner (**Chapter 6**) for the functional imaging measurements. The effect an external magnetic field has on bodily particles especially on protons is discussed next.

#### 2.2.1a Spin – T1

In a magnetic field environment a proton acts like a bar magnet with a north and a south pole, and spins around the axis of the magnetic field ( $B_0$ , **Fig. 2.1**). In nuclei that have an even number of protons, the protons will spin in opposite direction cancelling each other out. Therefore, in MRI only nuclei that have odd numbers of protons can be measured. Hydrogen (H) has a single proton and is highly distributed in the human body (63%). In hydrogen each proton generates a magnetic field and

the nucleus has a magnetic dipole moment. The axis of the proton's dipole can be in two energy levels: low (i.e. same direction as  $B_0$ ) or high (i.e. opposite the direction of  $B_0$ ) with a ratio of  $10^6+1:10^6$ , respectively. This slight bias toward the low energy level is enough to generate a net magnetic field (which is the sum over all hydrogen magnetic moment) with its axis lined up with  $B_0$ . The time for the net magnetization to line up with the external magnetic field axis is measured in T1 units and is described as an exponential growth (after  $1 \cdot T1$  63% of protons have lined up with  $B_0$  axis). The T1 time unit depends on the electrical and chemical environment (e.g. the density of protons in the tissue) and the strength of the external magnetic field. The stronger the external magnetic field the shorter the T1 time is for a given tissue.



**Figure 2.1:** Energy states.

Magnetic field environment aligned protons spin axis to the axis of the field, each proton's spin have a direction generating a magnetic dipole. The direction can be aligned to the axis of the magnetic field in this case the proton will be in a low energy state or can be opposite to the direction of the external field than the proton will have a high energy state.

### 2.2.1b Spin precession, phase – T2

When a proton is placed in an external magnetic field, it begins to “wobble” or precess about the axis of that field, possibly due to gravity. Thus, in addition to its natural spinning about its own axis aligned with the external axis of  $B_0$ , it also starts to rotate about the axis of the external magnetic field (**Fig. 2.2**). Each proton has its own phase of rotation about the external field axis; therefore this precession does not affect the net field magnetization. As will be described later, following delivery of a radio frequency wave (i.e. perturbation of energy to the system) the protons' phase precessions about the  $B_0$  axis synchronize and the time for protons to return to an out of phase precession is termed T2. T2 is described as an exponential decay, with a much shorter time scale compared to T1, and is affected by the chemical and



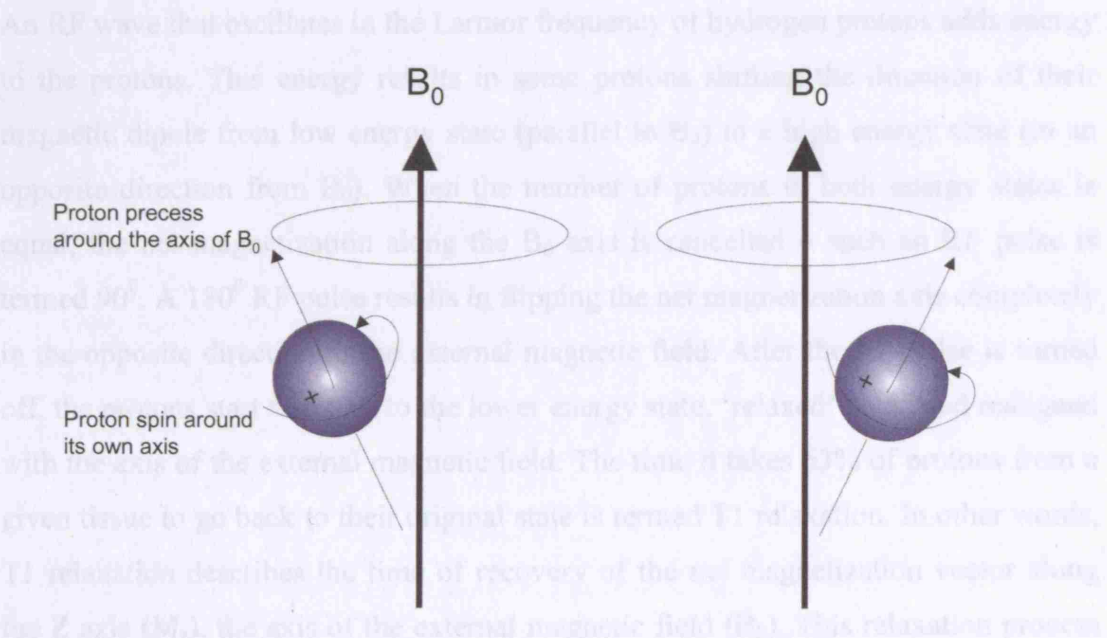
electronic environment of the hydrogen proton and by the strength of the external magnetic field. The frequency of proton precession around the external magnetic field axis is determined by Larmor's equation:

$$\omega = \gamma B_0$$

Where  $\omega$  is the angular precession frequency,  $\gamma$  is gyromagnetic ratio and  $B_0$  is a constant known for a given nucleus. In the case of hydrogen protons it is:

$$\gamma(\text{H}) = 42.6 \text{ MHz/Tesla}$$

Following Larmor's law, the precession frequency depends on the strength of the external magnetic field and the constant ratio for each nucleus. As the strength of magnetic field increases the precession frequency of the proton around the former axis increases as well.



**Figure 2.2** Proton precession in the presence of an external magnetic field.

The precession phase of each proton is random, they cancelled each other out, and the net magnetization field axis is as of  $B_0$ .

### 2.2.2 Radio frequency pulse

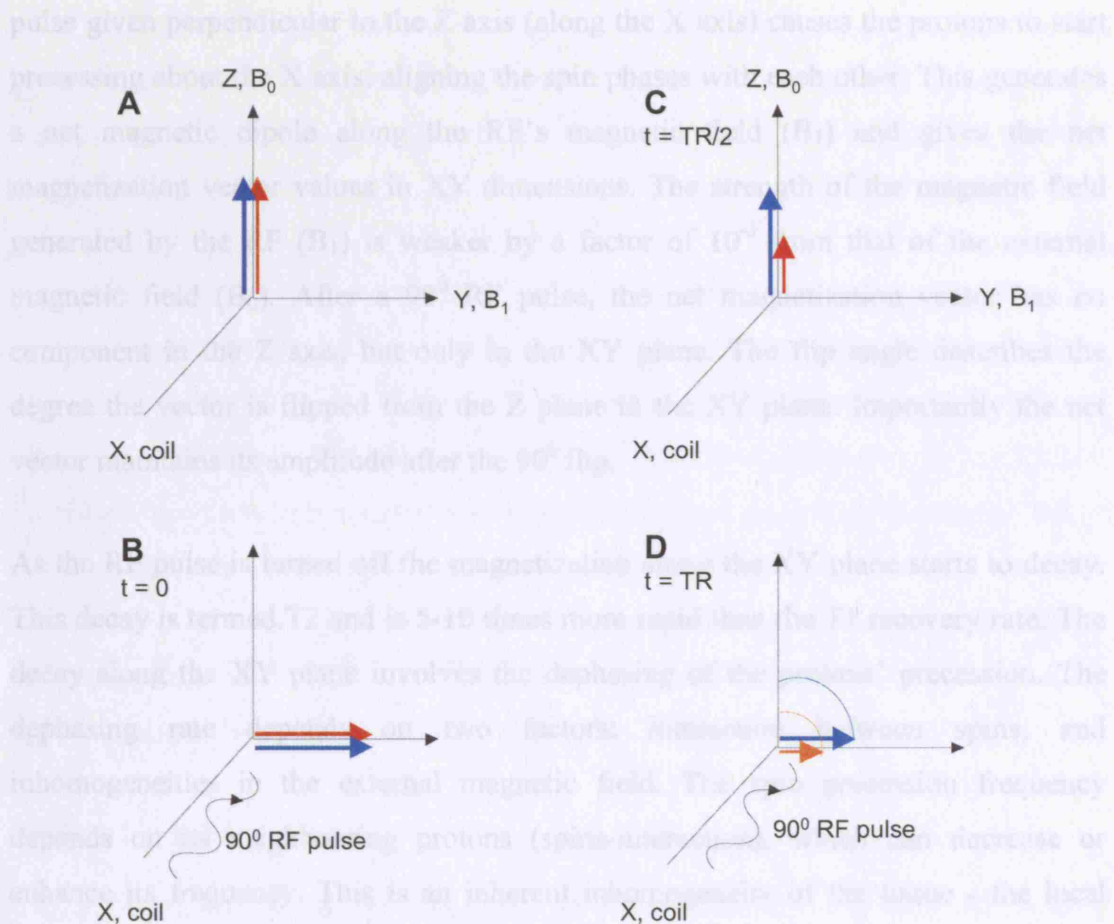
A radio frequency (RF) pulse is an electromagnetic wave. It is used to perturb the net magnetization equilibrium, by introducing energy to the system. The state of the net magnetic field prior to the RF is known, based on the knowledge about the external field, with a given direction ( $B_0$ ) and a given strength that affects the T1 and T2



times of given substance. The net magnetization can be described as a vector ( $M$ ) in 3D space with a Z axis aligned with the external magnetic field axis,  $B_0$  (**Fig. 2.3**). At equilibrium, the net magnetization vector ( $M_0$ ) is positive in the Z axis and is zero on the X and Y axes. In order to perturb the hydrogen protons by the RF pulse (i.e. change the net magnetization vector), the frequency of the pulse should resonate with the precession frequency of the protons. Resonance is established if the protons precess at the same rate as the RF oscillates. As described above this rate is known and can be calculated using Larmor's equation. The RF pulse, given in the appropriate frequency affects the net magnetization in two orthogonal ways that are discussed next. RF pulses are submitted along the X axis.

### **2.2.2a T1 relaxation**

An RF wave that oscillates in the Larmor frequency of hydrogen protons adds energy to the protons. This energy results in some protons shifting the direction of their magnetic dipole from low energy state (parallel to  $B_0$ ) to a high energy state (in an opposite direction from  $B_0$ ). When the number of protons in both energy states is equal, the net magnetization along the  $B_0$  axis is cancelled – such an RF pulse is termed  $90^\circ$ . A  $180^\circ$  RF pulse results in flipping the net magnetization axis completely in the opposite direction to the external magnetic field. After the RF pulse is turned off, the protons start to return to the lower energy state, 'relaxed' back, and realigned with the axis of the external magnetic field. The time it takes 63% of protons from a given tissue to go back to their original state is termed T1 relaxation. In other words, T1 relaxation describes the time of recovery of the net magnetization vector along the Z axis ( $M_z$ ), the axis of the external magnetic field ( $B_0$ ). This relaxation process involves giving back the energy obtained from the RF pulse and its rate depends to some extent on the density of mobile protons in the tissue. Therefore T1 relaxation of white matter is shorter than grey matter, which is shorter than CSF.



**Figure 2.3:** T1 weighted image.

This is a graphic representation of the of a 3 dimensional space, with Z representing the axis of the external magnetic field ( $B_0$ ), Y the magnetic field that is generated after an RF pulse is submitted ( $B_1$ ) and X is the axis along which the RF pulse is transmitted and the signal is recorded (the coil). Blue represent the net magnetization vector of a tissue with a short T1, i.e. fast recovery rate, typical for white matter. Orange represent a tissue with longer T1 i.e. slower recovery rate, typical for grey matter. **A.** At the equilibrium state, prior to the transmission of the first RF pulse, all tissues net magnetization are align with the external magnetic filed ( $B_0$ ). They have similar amplitude along that axis with no components at the XY plane. **B.** At  $t = 0$ , a  $90^\circ$  RF pulse is transmitted that flip the net magnetization of all tissues to the XY plane. At  $t = 0$  all tissues have similar amplitude in the XY plane with no component at the Z axis. **C.** After switching off the RF pulse, the net magnetization vector of each tissue start to recover at its own T1 rate, generating differences between them, with each tissue having a different amplitude along the Z axis. **D.** At  $t = TR$  a second RF pulse is transferred, flipping the net magnetization vector back to the XY plane. This time the differences in the recovery rate influence the amplitude of the vector in the XY plane. larger signal intensity is received from the blue tissue, i.e. white matter compared to the orange tissue, i.e. grey matter.

### 2.2.2b T2 & T2\* relaxation

The effect of the RF pulse on the net magnetization vector in the X and Y dimensions relates to T2 time. At equilibrium,  $M_{xy}$  equals zero, as protons randomly precess around the Z axis (i.e.  $B_0$ ) cancelling any net component along the X and Y axes. Thus at equilibrium the net magnetization vector does not precess. An RF

pulse given perpendicular to the Z axis (along the X axis) causes the protons to start precessing about the X axis, aligning the spin phases with each other. This generates a net magnetic dipole along the RF's magnetic field ( $B_1$ ) and gives the net magnetization vector values in XY dimensions. The strength of the magnetic field generated by the RF ( $B_1$ ) is weaker by a factor of  $10^{-3}$  from that of the external magnetic field ( $B_0$ ). After a  $90^\circ$  RF pulse, the net magnetization vector has no component in the Z axis, but only in the XY plane. The flip angle describes the degree the vector is flipped from the Z plane to the XY plane. Importantly the net vector maintains its amplitude after the  $90^\circ$  flip.

As the RF pulse is turned off the magnetization along the XY plane starts to decay. This decay is termed T2 and is 5-10 times more rapid than the T1 recovery rate. The decay along the XY plane involves the dephasing of the protons' precession. The dephasing rate depends on two factors: interaction between spins, and inhomogeneities in the external magnetic field. The spin precession frequency depends on its neighbouring protons (spins-interaction), which can decrease or enhance its frequency. This is an inherent inhomogeneity of the tissue - the local environment influences the hydrogen protons and is termed T2. In respect to brain tissues: CSF has a longer T2 than grey matter's T2, which is longer than white matter's T2. The external magnetic field inhomogeneity exposes protons in different locations to slightly different magnetic field strength which affect their precession frequency, leading to differences in the decay rate of the magnetic field  $B_1$ . The effect of both - the inherent characteristic of the tissue (T2) and the inhomogeneity in the external magnetic field - is termed T2\* relaxation.

### ***2.2.3 Receiver coils and tissue contrast***

T1 and T2\* relaxation are orthogonal phenomena that describe the behaviour of the net vector magnetization (M) after RF pulse has been administered. Though independent, they both affect the net magnetization vector simultaneously. The oscillation in the net magnetization vector induces an electromagnetic wave which is the signal recorded in the MRI receiver coils. Usually these coils transmit the RF pulse and then receive the signal back. The coil is an electric wire, such that when an alternating electric current (AC) is run through it, it generates an electromagnetic

wave. In the same way, when this wire is exposed to an alternating magnetic field it generates an electric current that can be recorded. The electromagnetic wave, the RF pulse, is transmitted along the X axis and the received signal in the coil is encoded along the same axis.

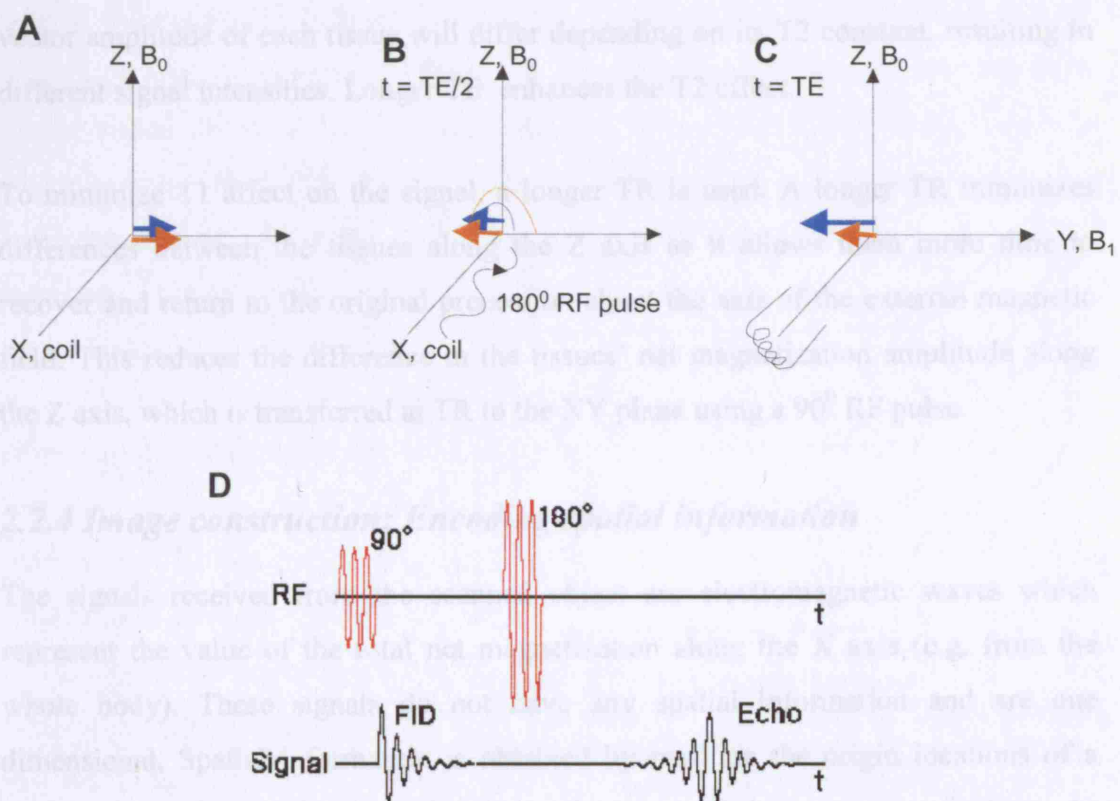
In an ideal world the received signal would have the same amplitude as the RF pulse. However, because of spin dephasing, which mainly affects the net magnetization vector along the XY plane (i.e. the  $T_2^*$  relaxation), the received signal becomes weaker and weaker. This phenomenon is termed free induction decay (FID). Therefore, the time relation between transmitting and receiving the signal has a critical effect on the amplitude of the signal and its sensitivity to  $T_1$  and  $T_2^*$  relaxations. The time unit between two RF pulse transmissions for a single slice is called repetition time (TR) while the time between the transmission of the RF pulse and receiving the signal is called echo time (TE).

### 2.2.3a $T_1$ weighted image

A first transmitted  $90^\circ$  RF pulse flips the net magnetization vector from the Z plane to the XY dimension, while maintaining the amplitude, which is equal to all tissue types at equilibrium (**Fig. 2.3a**). As the RF pulse is turned off, the net magnetization vector starts to build itself back around the axis of the external magnetic field (i.e Z axis). The rate at which this happens depends on the  $T_1$  constant of a given tissue. Therefore, after a given time, tissues will differ in the extent that their net magnetization vectors have recovered around the external magnetic field (**Fig. 2.3c**). Eventually, all tissues' net magnetization vectors will align with the external magnetic field. But, if another  $90^\circ$  RF pulse is transmitted before the tissues' net magnetization have fully recovered, then the net magnetization vector's amplitude along the XY plane will differ, depending on how much they have recovered along the Z axis (**Fig. 2.3d**). A short TR (the time between two RF pulses) enhances the differences between tissues in their  $T_1$  relaxation. A more intense signal will be recorded for tissues with a shorter  $T_1$ , i.e. with a faster recovery rate; thus white matter will be brighter than grey matter and grey matter brighter than CSF.

As was described before, after the RF pulse is turned off, the net magnetization vector along the XY plane starts to decay due to spin dephasing. To minimize the

effect of the  $T_2^*$  relaxation component of the measured signal, the signal is recorded with the shortest delay as possible. A short TE (time between transmitting RF pulse and receiving signal) minimizes the effect of  $T_2^*$  relaxation. The problem is that there is a minimum interval between administration of the RF pulse and receiving a signal by the same coil - due to the rapid  $T_2^*$  a lot of signal is lost by the time of receiving. To stretch the time, an additional RF pulse is used, a  $180^\circ$  pulse. The role of this RF pulse is to rephase or refocus the signal in the XY plane. It is turned on after half a TE has past, i.e. after half of the dephasing process has occurred. Following the  $180^\circ$  pulse the protons flip the direction of their precession, leading the fast precessing protons to be 'behind' the slow precessing ones. After another half TE, they will close the gap and all protons will precess in phase and the signal will be recovered to its maximum in the XY plane. The signal received at that point is described as an echo for the original signal.



**Figure 2.4** T1 spin echo

**A.** After the second RF pulse is switched off ( $T(TE+TE/4)$ ) the signal starts decaying due to the dephasing. This decay affects the net magnetization vector along the XY plane. **B.** In order to recover the signal an additional RF pulse with  $180^\circ$  flip angle is administered usually after  $TE+TE/2$ . This RF flips the net magnetization vector. **C.** After this RF is switched off the protons' frequency precession starts to change in the opposite direction. After  $TE/2$  they all become in phase again, and the original amplitude along the XY plane is recovered i.e. its echo. **D.** A graphic demonstration of a T1 spin echo sequence.

### **2.2.3b T2\* weighted image**

In order to emphasize the T2 characteristics of a tissue rather than the T1, a different time relation between the TR and TE is used. Recall that T2 relaxation determines the time it takes for protons to dephase in a given tissue. As mentioned above its time scale is much shorter than T1 relaxation. T2 relaxation is the amplitude of the vector along the XY plane. After transmitting the  $90^\circ$  RF pulse, all the net magnetization vectors are flipped to the XY plane and have similar amplitude. The value of the net magnetization along the XY plane is given from the synchronizing of the protons precession about the Z axis. When switching the RF pulse off, the magnetization vector along the XY plane starts to decay. The decay rate depends on the tissue's constant T2 and is influenced by the inhomogeneities in the external magnetic field (together defined as T2\*). The component of the magnetic vector along the XY plane zeroes out at a T2\* rate. But if a signal is recorded just before, the magnetization vector amplitude of each tissue will differ depending on its T2 constant, resulting in different signal intensities. Longer TE enhances the T2 effect.

To minimize T1 affect on the signal, a longer TR is used. A longer TR minimizes differences between the tissues along the Z axis as it allows them more time to recover and return to the original precession about the axis of the external magnetic field. This reduces the difference in the tissues' net magnetization amplitude along the Z axis, which is transferred at TR to the XY plane using a  $90^\circ$  RF pulse.

### **2.2.4 Image construction: Encoding spatial information**

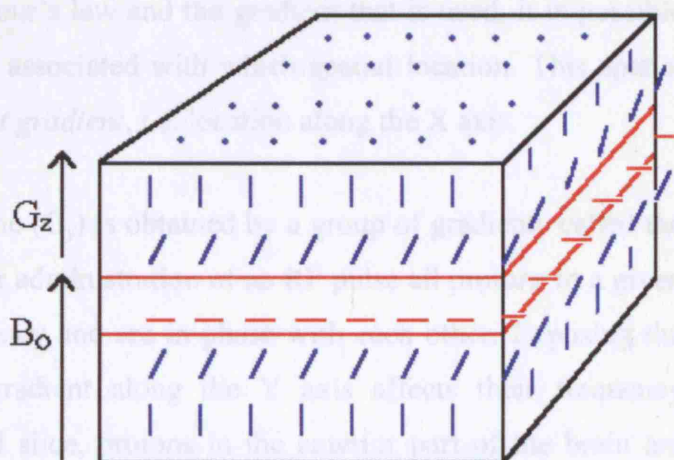
The signals received from the scanned object are electromagnetic waves which represent the value of the total net magnetization along the X axis (e.g. from the whole body). These signals do not have any spatial information and are one dimensional. Spatial information is obtained by marking the origin locations of a signal, using frequencies, i.e. the precessing rate of the net magnetization. As described above this precession is determined by Larmour's law, and depends on the strength of the magnetic field. Thus a gradient change of the external magnetic field strength introduces corresponding gradient changes in the frequency of precession of protons along this gradient. This basic principle is used in three different ways to provide spatial information in 3D space.



**Slice-Select gradient** - spatial information that relates to the slice is described as the spatial location on the Z axis ( $G_z$ ). When selecting slices for image acquisition a gradient coil is used to generate a gradual change in the external magnetic field and is applied perpendicular to the slices orientation. The gradient is zero in the middle and increases or decreases the magnetic field strength towards the edges. As the gradient is activated, protons along its axis change their frequency precession accordingly (**Fig. 2.5**). For example, when acquiring pure axial slices the cerebellum experiences a weaker magnetic field compare to the central sulcus, the former's protons would precess more slowly compared to those in the latter. Recall, that in order to 'inject' energy to the protons the RF pulse should match their frequency (i.e. resonant with them). Using RF with limited frequency band perturbs only protons that their frequency precession matches that of the RF. Other protons that experience a different magnetic field, (because of the gradient) and have different frequencies precession will not be affected by this RF. Therefore, the net magnetization from protons in other slices remains zero in the XY dimension and they do not contribute to the signal recorded by the receiving coil (**Fig. 2.5**). The slice thickness is determined by the frequency band used for each RF pulse, such that a larger bandwidth would lead to a thicker slice.

An important attribute of the frequency spectrum of the RF pulse is that it does not have sharp edges. This may results in protons being excited twice by two different RF pulses leading to a mismatch in spatial location. To avoid such overlaps a gap is used between the frequency

bands of each RF pulse. This gap is chosen based on the shape of the RF spectrum and is termed the distance factor. In the experiments described in this thesis the distance factor was in the range of 50 - 75% of the slice thickness.



**Figure 2.5: Slice-select gradient**

Using magnetic field gradient along the  $B_0$  axis (i.e. Z) will change the frequency precession of the protons depending on the magnetic field they experience. An RF pulse applied perpendicular to the  $B_0$  axis will affect only protons with matching frequencies, here for example along the red slice.

All protons in a given slice experience the same magnetic field strength, due to the *select-slice gradient*, and they all precess in the same frequency. Therefore, a received signal would have a uniform frequency and its amplitude would be the sum of the net magnetization vector along this slice. The signal amplitude will be dependent on the tissues in that slice and whether we measure T1 or T2\* relaxation time. But this signal does not have any information regarding the spatial distribution of the different amplitudes within a slice. To establish a location in the x axis another gradient is applied - the ***read-out gradient*** (known also as the frequency-encoding gradient) along the X axis ( $G_x$ ). Here again, different frequencies are associated with different spatial locations within a slice, but this time the frequency location-marking affects the received and not the transmitted signal. In an axial (transverse) slice the *read-out gradient* is spread from left to right. This gradient is turned on when a signal is received at TE. It causes different protons within a slice to experience different magnetic fields and therefore to change their frequency precession in correspondence. After a *read-out gradient* is applied the received signal does not have a uniform frequency, but is composed from different frequencies, each with its own amplitude. Based on Larmour's law and the gradient that is used, it is possible to calculate which frequency is associated with which spatial location. This spatial information is along the *read-out gradient*, i.e. location along the X axis.

Spatial location along the Y plane ( $G_y$ ) is obtained by a group of gradients called the ***phase-encoding gradients***. After administration of an RF pulse all protons in a given slice precess at the same frequency and are in phase with each other. Exposing the protons to a magnetic field gradient along the Y axis affects their frequency precession such that in an axial slice, protons in the anterior part of the brain are exposed to a stronger magnetic field and therefore precess quicker than protons in the posterior part of the brain. Along this gradient protons are in-phase when they are exposed to the same magnetic field and out-of-phase with protons that are exposed to a different gradient. When this gradient is turned off all protons in the slice return to the same precession frequency, but they maintain the phase relation between them. But only one signal is received from an excited slice, which is not enough to calculate the spatial origin of the various frequency components. Different angles of the *phase-encoding gradient* are used to obtain enough phasing information to calculate the location, or the resolution along the Y axis.

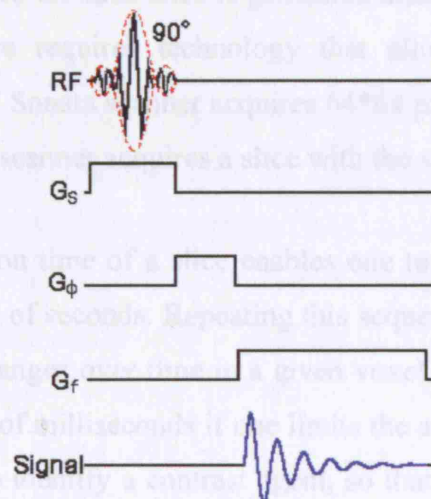


All protons in a given slice experience the same magnetic field strength, due to the *select-slice gradient*, and they all precess in the same frequency. Therefore, a received signal would have a uniform frequency and its amplitude would be the sum of the net magnetization vector along this slice. The signal amplitude will be dependent on the tissues in that slice and whether we measure T1 or T2\* relaxation time. But this signal does not have any information regarding the spatial distribution of the different amplitudes within a slice. To establish a location in the x axis another gradient is applied - the ***read-out gradient*** (known also as the frequency-encoding gradient) along the X axis ( $G_x$ ). Here again, different frequencies are associated with different spatial locations within a slice, but this time the frequency location-marking affects the received and not the transmitted signal. In an axial (transverse) slice the *read-out gradient* is spread from left to right. This gradient is turned on when a signal is received at TE. It causes different protons within a slice to experience different magnetic fields and therefore to change their frequency precession in correspondence. After a *read-out gradient* is applied the received signal does not have a uniform frequency, but is composed from different frequencies, each with its own amplitude. Based on Larmour's law and the gradient that is used, it is possible to calculate which frequency is associated with which spatial location. This spatial information is along the *read-out gradient*, i.e. location along the X axis.

Spatial location along the Y plane ( $G_y$ ) is obtained by a group of gradients called the ***phase-encoding gradients***. After administration of an RF pulse all protons in a given slice precess at the same frequency and are in phase with each other. Exposing the protons to a magnetic field gradient along the Y axis affects their frequency precession such that in an axial slice, protons in the anterior part of the brain are exposed to a stronger magnetic field and therefore precess quicker than protons in the posterior part of the brain. Along this gradient protons are in-phase when they are exposed to the same magnetic field and out-of-phase with protons that are exposed to a different gradient. When this gradient is turned off all protons in the slice return to the same precession frequency, but they maintain the phase relation between them. But only one signal is received from an excited slice, which is not enough to calculate the spatial origin of the various frequency components. Different angles of the *phase-encoding gradient* are used to obtain enough phasing information to calculate the location, or the resolution along the Y axis.

To summarize, the spatial location information regarding the signal origin is achieved by applying three different magnetic field gradients (**Fig. 2.6**). The first (*slice-select*  $G_z$ ) determines the protons that are affected by the RF and change their net magnetization to the XY axes, the second (*phase-encoding*  $G_y$ ) with various gradient angles affects the phase precession of protons and the third (*read-out*  $G_x$ ) affects the protons frequency precession. The two latter gradients are extracted from the received signals.

The received signals are encoded in data space, termed K-Space. Each slice is encoded on a single K-space. In K-space signals are organized in rows following their phase and the  $G_y$  angle used before they were encoded. A Fourier transform is used to transform the image to spatial space from K-Space, as each frequency and phase originates from a different spatial location.



**Figure 2.6** – Magnetic gradients applied to encode spatial information

This is a simplified example of a sequence. The x axis represent time, RF pulse is applied while the *slice select gradient* ( $G_s$ ) is on, therefore perturbing only protons within a given slice. After it is switch off a *phase encoding gradient* ( $G_\phi$ ) is used to synchronise the precession phase of protons along the Y plane. After it is switch off the last *read-out gradient* ( $G_r$ ) is applied and here the location along the X axis is marked using different frequencies. The signal is recorded after TE, after the last gradient is switched off. This sequence is repeatedly applied in each slice with different *phase encoding gradients*. In the EPI sequence the processes is faster because only one RF pulse is applied for the various *phase encoding gradients*.

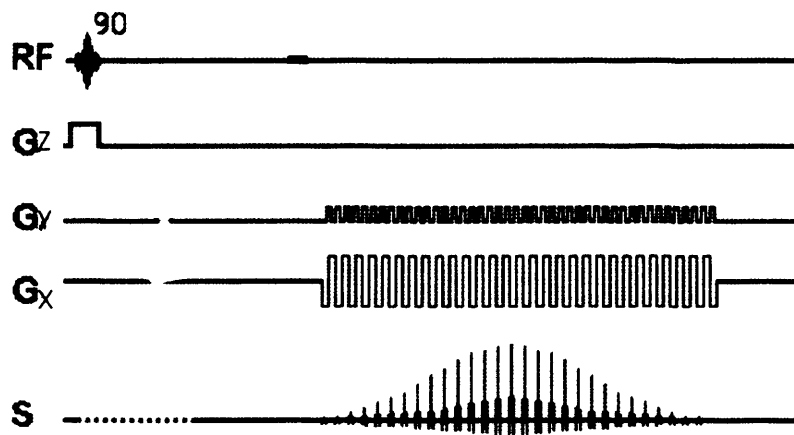
In the current studies, reconstruction of the spatial location of the functional images from K-space was done using TBR methods developed by Josephs et al. (2001). This method uses trajectories images acquired periodically using a phantom object in each of the scanners. Based on these images inhomogeneities in the magnetic field are

measured and used to correct the way the spatial information is coded in K-space. The advantage of using TBR for image reconstruction is that it corrects for ghosting effects and partly for distortions in the final image.

### ***2.2.5 Echo Planner Imaging (EPI) – The BOLD***

Echo planer imaging (EPI) belongs to the family of fast scanning techniques. This sequence is most commonly used for functional imaging experiments, and was used in all fMRI experiments reported in the current thesis. EPI is mostly affected by T2\* relaxation. This sequence is unique, since a whole slice is acquired at a single shot, after a single RF pulse. In other sequences, every phase-encoding gradient marking the signal origin location on the Y axis, is used with a new RF pulse. Here, a single RF pulse is used followed by a sequence of phase-encoding gradients with different angles intermixed with a read-out gradient which records the signal (**Fig. 2.7**). In other words, K-space for each slice is generated after one RF pulse. As T2\* decay is rapid, this measure requires technology that allows rapid on-off switching of gradients. The 1.5T Sonata scanner acquires 64\*64 pixels of a single slice in 90msec, and the 3T Allegra scanner acquires a slice with the same resolution in 65msec.

The rapid acquisition time of a slice enables one to acquire a whole volume of the brain within couple of seconds. Repeating this sequence over and over again enables measurement of changes over time in a given voxel. The sample rate is in the order of seconds, or tens of milliseconds if one limits the acquisition to one slice. The next important step is to identify a contrast agent, so that its changes are associated with tissues function.



**Figure 2.7** – Echo planner imaging sequence

This is a simplified example of an EPI sequence. 90° RF pulse is applied while the *slice select gradient* (G<sub>z</sub>) is on, therefore perturbing only protons within a given slice. After it is switch off a set of intermixed *phase encoding* (G<sub>y</sub>) and *read-out* (G<sub>x</sub>) gradients are applied to provide spatial location information along the Y and X axes correspondingly. The signal is read after each *read-out gradient*.

T2\* relaxation as discussed above is affected by spin-spin interaction and inhomogeneities in the magnetic field. The latter can arise from a non-homogenous external magnetic field, but is also affected by the different magnetic susceptibility of different substances in the brain. Substance susceptibility is determined by the number of unpaired electrons in it. Paramagnetic substances become magnetized in the presence of an external magnetic field and have shorter T1 and T2 relaxation times and make the signal look darker. An important paramagnetic material that affects the electromagnetic signal recorded in EPI sequence is deoxyhemoglobin. Blood with more deoxyhemoglobin will have a darker signal compared to blood with oxygenated haemoglobin. Ogawa and Lee (1990) were the first to describe this change of signal in blood vessels, and they termed the contrast blood-oxygenation-level-dependent (BOLD). Changes in the BOLD are the parameters measured in fMRI. The assumption is that changes in blood oxygen are coupled with neural activity. The exact origin of the BOLD contrast is not clear and is discussed next.

### 2.2.6 The origin of the BOLD response

The origin of changes in blood oxygen concentration is at the heart of the assumptions that connect neural activity to the measured T2\* values. It is assumed

that neural activity changes the relative concentration of oxygenated and deoxygenated blood and that in turn affects  $T2^*$  values. Presence of deoxyhaemoglobin causes a decrease in  $T2^*$  signal compared to oxyhaemoglobin, due the paramagnetic nature of the former that generates inhomogeneities in the local magnetic field that increases the dephasing rate.

An intriguing question then is, why in functional imaging experiments the BOLD effects observed reflect increases, rather than decreases in signal, as would be expected after oxygen consumption by the active neurons? It has been suggested that this enhanced signal is due to cerebral blood flow that overcompensates for the decrease in oxygen, delivering an oversupply of oxygenated blood to the activated region. One explanation for this oversupply might be that it compensates for the inefficient, passive oxygen diffusion that occurs at high flow rates (Buxton and Frank, 1997; Hyder et al., 1998). If this is the case than oxygenation supply is tightly coupled to neural activity (Logothetis and Wandell, 2004).

The time course of the BOLD response is often referred to as the haemodynamic response function (HRF). It is typically described as follows: increases in BOLD start roughly 2sec after stimulus presentation, it peaks at 6-9sec after stimulus onset and returns to baseline within 20-30sec. In some cases the BOLD response is described as having a post-stimulus undershoot (Kwong et al., 1992). There is no straight forward linear relation between BOLD response and stimulus duration. It has been shown that a linear relation can give good approximations that predicted BOLD responses if considered separately for brief and long (>6sec) duration (Rees et al., 1997). Another issue to keep in mind is that the HRF is potentially heterogeneous across different brain regions and between subjects for a given cortical region (Birn et al., 1992; Menon et al., 1992). These last two points are particularly important issues, as quantitative tests rely on an adequate modelling of the BOLD response.

One critical concern relates to the neural processes that the BOLD response reflects. This issue is especially important if we want to compare findings from different imaging modalities. In the case of the current thesis I compare BOLD and EEG responses (see **Part IV**). Several studies have shown a linear relation between the BOLD response and the mean extracellular field potential (Logothetis et al., 2001).

Mean extracellular field potential has two components: multiple units spike activity (MUA) and local synaptic voltage which affects the local field potential (LFP). The MUA measures regional neuronal spiking and the LFP measures slow waveforms, including synaptic potentials, after potentials of somato-dendritic spikes and voltage-gated membrane oscillations. The LFP reflects the input signals but not the action potential carried by the principle neurons (the output), as does the MUA. These two components are represented as different frequencies in the mean extracellular field potential, with high frequencies reflecting MUA, as their responses are rapid, while low frequencies reflect the LFP, as it is a much slower response. As expected these two components are not independent, and LFP affects MUA. But there are cases where these two measurements can be dissociated. Logothetis et al. (2001) show in striate cortex for 12 and 24sec visual stimulation MUA (i.e. neurons spike activity – output) increases and return to baseline within 2.5sec. In contrast, LFP (i.e. input for the region) remained elevated for the entire stimuli duration. The BOLD response measured simultaneously from the same cortical site, also varied with stimulus duration. This suggests that BOLD response reflects LFP and not MUA (Logothetis et al., 2001). Therefore, importantly, the BOLD correlates with input of a signal to a region rather its output.

In support of this it has been demonstrated that vascular density is highly correlated with synaptic density rather than with neuronal density (Duvernoy et al., 1981; Schuz et al., 1989). In addition it has been suggested that blood flow is regulated by pre-synaptic activity and neurotransmitter cycling via glial cells (Araque et al., 1999). Thus, blood flow is controlled by mechanisms that predict energy consumption and not by mechanisms that measure the actual consumption (Logothetis and Wandell, 2004).

Two important concerns have to be kept in mind when interpreting BOLD response. The first is that given the heterogeneous nature of the HRF, direct comparison of BOLD responses between different brain regions is not possible, i.e. one can never infer a main effect of a region, but only interactions with an experimental manipulation. In addition there is no simple correlation between the amplitude of BOLD response and underlining neuronal activity, therefore inferences should be

made relatively, by comparing BOLD responses for different conditions in a given cortical region.

### ***2.2.7 Artefacts in MRI***

MRI, as any other imaging modality, is susceptible to artefacts. In this section I will briefly review the possible artefacts that can occur which in MRI can be introduced through any stage of the image acquisition. This section focuses on artefacts in the EPI sequence and the strategies used here to minimize them.

**Inhomogeneities in the external magnetic field** are a major source of concern, mainly for imaging sequences that aim to measure the T2 relaxation, such as the EPI. Spatial localization is based on frequencies markers which are calculated using knowledge of the magnetic field environment of the voxel. Therefore, inhomogeneities cause uncontrolled changes in that environment and can lead to mismatch in localization. Such inhomogeneities may rise from the quality of the magnet, the presence of ferromagnetic and paramagnetic substances, the presence of nearby electromagnetic fields etc. For example, a coin, being a ferromagnetic substance that was forgotten in a subject's pocket can generate strong inhomogeneity in the magnetic field. Similarly, electric currents in the vicinity of the magnet, such as a current flowing through electrodes recording skin-conductance or a video projector presenting the stimuli for the subjects, can generate inhomogeneities in the field as well.

Biological causes (such as air pockets) caused local inhomogeneities and are termed 'susceptibility artefacts'. They occur at interfaces of tissues with differing magnetic susceptibilities, such as tissue-air and tissue-fat. One important location where these artefacts are common is in vicinity to paranasal sinuses, where it causes loss and mismapping of the signal. This artefact is prominent in regions that are of most interest in the current thesis, namely anterior temporal cortices including the amygdala, fusiform gyrus, and anterior temporal pole.

This artefact can be dealt with by optimizing the acquisition procedure, or by using information about the field inhomogeneities in the reconstruction phase (Hutton et al., 2003, 2005). Here, I optimize the acquisition procedure as the later technique was

not operational at the time I acquired my data. Minimizing the susceptibility artefact arising from the paranasal sinuses was done by tilting the slice-select gradient,  $-30^{\circ}$  along the axial-coronal axis, such that within a slice it minimized the interface between tissues and air. Tilting the slices at such an angle has been shown to be the most efficient way to reduce artefacts in the above region of interests, while maintaining the total time acquisition per slice (Diechman et al., 2001).

Partial volume is another artefact that occurs at interface of different tissues. It is a result of the limited spatial resolution. In cases where a single voxel samples signal from two different tissues it is impossible to localise the true origin of the signal. The way to minimize this artefact is by reducing the voxel size. This is the case for example, on voxels that are located on border of the fusiform gyrus and the superior cerebellum,

Artefacts originating from the subjects mostly relate to **head movement and blood flow**. Both can cause mismapping due to changes in location in respect to the magnetic gradients. In the case of fMRI, the problem is more severe, as measurements are taken over time and the analysis is based on testing signal change in a given voxel over time. When the subject moves, one may end up testing signal change between voxels over time rather than within a voxel. This potential problem is dealt with offline, using pre-processing procedure such as realignment, unwarping and smoothing and will be described latter in more details.

## **2.3 USING fMRI FOR COGNITIVE NEUROSCIENCE RESEARCH: PROS AND CONS.**

In the last decade functional MRI has become one of the most commonly used tools in cognitive neuroscience, especially in studies involving humans. A typical experiment involves scanning volunteers using MRI while presenting them with different stimulation and asking them to perform various tasks regarding these stimuli. In the following paragraph I will describe the pros and cons of this technique.



### ***2.3.1 Safety issues***

One of the most attractive features of MRI is its non-invasive nature. MRI is an imaging technique which relies on natural agents in our body (i.e. hydrogen), and in the case of fMRI on a natural changes that occur in the blood (i.e. BOLD). Moreover, it does not expose subjects to high radiation, as it uses very low frequencies (within the range of radio frequencies) to perturb the system. Therefore, the low risk on the human volunteers participating in the experiments means there is no limitation on time or number of times they can be scanned.

### ***2.3.2 Spatial resolution***

The spatial resolution of fMRI is in the order of millimetres. A voxel of 3\*3\*3 mm in the cortex is estimated to contain about 30 thousand neurons (Sholl 1956). Therefore fMRI measures neuronal population response, and cannot distinguish between different neuronal responses within the same voxel. Moreover vascular dilatation that is responsible for increase in blood flow and is evoked by neural activity, has been shown to propagate in a retrograde fashion to upstream arterioles located outside the activated area (Iadecola et al., 1997), reducing the resolution even more.

fMRI-adaptation (Grill-Spector and Malach, 2001) has been suggested as a possible experimental paradigm to increase the spatial resolution of fMRI to the sub-voxel level. In this method, reduction in BOLD response is measured as a function of stimuli repetition. Under the assumption that observed repetition-related decreases are specific characteristics of single neurons responses, and hence depict neuronal responses at a sub-voxel level. The repetition related decrease paradigm was used here in three of the reported studies (see **Chapter 6** and **Part III**).

fMRI as opposed to single cell and intracranial recording can be used to measure the BOLD response from the entire brain, and therefore to investigate connections and network activation across different regions. In comparison to other imaging methods such as PET and SPECT, fMRI has a much finer resolution, with the former resolution being in the order of tens of millimetres. For EEG and MEG there is no simple way to spatially localize the origin of the signal that is recorded from the

scalp, as it involves a transformation from 2D data space to 3D space. Therefore EEG cannot easily access spatial information.

### ***2.3.3 Temporal resolution***

The BOLD response changes as described before follow the haemodynamic function. The HRF typically starts after 2sec and peaks 6-9sec from stimuli onset. The HRF is a low pass filter for any neuronal response in the temporal domain. As neuronal responses and connections between regions are in the order of milliseconds the BOLD is in the order of seconds, any temporal differences within or between regions are ‘washed’ out. Moreover, due the heterogeneous nature of HRF, any differences between regions in onset or time to peak of the BOLD response cannot be conclusively attributed to temporal differences in neuronal activity, but could be due to difference in vascular anatomy, and blood supply between the regions.

As described before, for brief stimulation HRF has approximately linear relation with the number of stimuli presented. Based on this forward model, time resolution can be increased beyond HRF resolution limitations. Modelling the HRF response under the assumption of linearity allows experimental manipulations such as event-related design. In these contexts stimuli onset asynchronous (SOA) is in the order of 2-3sec. Event related designs are used in all the reported experiments here.

EEG and MEG have time resolution in order of milliseconds and are therefore better than fMRI. Therefore, a combination of these techniques and fMRI measurements, as done in **Part IV** is a powerful way to get high temporal resolution information and high spatial resolution information, respectively.

## **2.4 ANALYSIS OF FUNCTIONAL MRI TIME SERIES**

So far I have discussed the principles that underlie data acquisition specifically focusing on functional MR images (fMRI). fMRI measured using EPI sequence is sensitive to BOLD. As mentioned before the absolute value of the BOLD response is hard to interpret and therefore most neuroimaging studies, including the ones

reported here, compare the BOLD response under different experimental conditions and rely on classical statistical inference. The results are presented as 3D statistical maps. In the current thesis all experiments were analysed using SPM2, a Matlab based toolbox for statistical image analysis developed in Wellcome Department for Imaging Neuroscience, University College London.

The first step in SPM2 is to pre-process the data, which includes correcting for spatial and temporal distortions, remapping the data to a conventional space (i.e. the MNI) and spatial smoothing. The second step in SPM2 is to generate a model that best explains the observed data. Then predictions are made regarding the expected *differential* BOLD response. These predictions can be statistically tested in the level of single subjects or across subjects. In the current thesis comparisons were made only across subjects using random effect models. This enables inferences to be drawn at the population level. Therefore, statistical tests are discussed only in the context of comparison across subjects.

### ***2.4.1 Image pre-processing***

#### **2.4.1a Spatial realignment and unwrapping**

Spatial realignment deals with artefacts that are caused by head movements. Changes in signal intensity in a given voxel due to head movement can affect the results in two ways. The first is when a subject's head movements correlate with experimental conditions confounding the experimental manipulation with head movement. In the second case head movements can cause artificial signal intensity change that introduces noise to the images and hence decreases the signal to noise ratio. To minimize head movement artefacts, participants are instructed not to move their head during scanning and their head is immobilized using soft pads. Nevertheless head movement in the order of millimetres occurs raising the need for retrospective motion correction.

The method for spatial registration used in SPM2 assumes that the shape of the brain does not change with head movement and therefore a rigid-body transformation can be used to model different head positions within the same subject (Ashburner and Friston, 2003a). However, it should be noted that as data acquisition in fMRI is

sequential, head movements during a single volume acquisition (i.e. within a TR) can lead to changes in the shape of subject head – an unwrap procedure is designed to deal with such artefacts and will be described later.

Spatial realignment procedure aligns all volumes (3D images) to the first volume, which is usually the one just after the signal has saturated (i.e. the sixth volume). The first volume then remains stationary (the reference) where as the others (the sources) are spatially transformed to fit it. Transformations involve mapping each voxel position in the source image to a corresponding position in the reference. As it is a rigid body transformation all voxels within a volume ‘move’ together, and their transformation can be described in a matrix with six parameters: three translations and three rotations. The source is then re-sampled at the new position. It is possible to skip the second step and not re-sample the image and to use the transformation information when the images are spatially normalized (i.e. transformed to the conventional MNI space). The advantage of the latter procedure is that it minimizes potential errors that can occur when images are being re-sampled. Such an approach was used in the experiment reported in **Chapter 6**.

Image transformation in SPM2 is implemented as a “pulling” rather than a “pushing” method (Ashburner and Friston, 2003a). In the former, a voxels new value is a pulled estimation based on information from neighbouring voxels in the original image, as opposed to having the voxel from the original image being “pushed” to its new location. One advantage of the above method is that it can cope with sub-voxel movements. Interpolation methods, i.e. ‘clever’ weighted average procedures, are used to estimate the new value of a voxel. In brief, SPM2 uses generalized interpolation, where a model of the image is generated as a linear combination of a set of B-spline basis functions. An image of basis function coefficients is produced. Estimation for re-sampling for each voxel in its new location involves computing the appropriate linear combination of these basic functions. The estimation is done iteratively, until a match with a-priori criterion is optimized. Transformations are computed sequentially for each dimension. After the six parameters are estimated re-sampling of the volume is preformed using rigid-body transformation methods.

**Unwrapping images at the realignment stage** - Head movement can lead to change in the shape of the head, due to miss-mapping of signal origin. Placing a head in a magnetic field causes geometric distortions. These distortions specifically depend on subject head shape and orientation. This means that apparent shape of the brain will vary with its position in the scanner, leading to movement related variance in fMRI time series. The distortion appears mostly in the Y dimension, as they mostly affect image reconstruction that is based on the *phase-encoding gradient*. These distortions cannot be corrected using rigid-body realignment. Therefore an unwrapped procedure is used based on the estimated movement parameters (Andersson et al., 2001). The critical parameter here is the geometric distortion in the field in any given time point. These field maps are estimated directly from the variance of the time series using the pitch and roll parameters. The new voxel value is estimated using the interpolation method of discrete cosine basis function. Voxels are re-mapped and the realignment procedure is applied again and this procedure iterates until it reaches a maximum likelihood solution (Andersson et al., 2001). I used an unwrapping procedure in the experiments reported in **Chapters 5, 7 - 9**.

#### **2.4.1b Temporal realignment**

fMRI data is acquired sequentially, thus generating temporal differences between different locations in the brain. For example, in one experiment reported here (**Chapter 5**) 44 slices were acquired with a 65msec time acquisition per slice in descending order, hence the most posterior slice was acquired about 2.7sec after the most anterior slice. This can introduce ‘apparent’ variability in the haemodynamic response measured from each slice and hence bias the results (Price et al., 1999; Friston et al., 1999).

One way to minimize the above problem is by adjusting the experimental design. Here, one needs to insure that stimulus onset asynchrony does not correlate with the time acquisition of a volume (i.e. TR), hence distributing stimuli presentation along the different time points of the volume acquisition. In addition SPM offers a method where images can be realigned in the temporal domain, i.e. aligning all data points within a volume in time. This is done by representing the signal at each voxel as linear combinations of sinusoids functions. The correction is done by ‘shifting’ the phase of these functions. Voxel value in time zero (time of the reference slice,

usually the middle one) is estimated based on sinc-interpolations along the time dimension.

It should be noted that this method is inefficient when sampling in time is too sparse i.e. long TR ( $>3\text{sec}$ ), and in the case of shorter TR ( $<2\text{sec}$ ) these temporal differences in the context of the haemodynamic response are assumed to be negligible. Realignment in the temporal domain was done in experiments reported in **Chapters 5, 7 - 9**.

#### **2.4.1c Spatial normalization**

Spatial normalization aligns all images into an international coordinate space. This allows comparison between subjects, averaging across subjects and standardisation of the data space to allow comparison between labs. SPM2 uses the Montréal Neurological Institute (MNI) images as templates. These templates' orientation roughly corresponds to Talairach coordinate space, with the anterior commissure being roughly at the centre (0,0,0); the y axis along posterior anterior axis with posterior commissure being at (0,y,0). The x axis increases from left to right, and the z increases from bottom to top of the brain. The MNI templates were generated by averaging ~152 healthy brains that have been transformed to Talaraich space using only affine transformations (i.e. linear transformation) and smoothed with an 8mm FWHM. It should be noted that the MNI and Talaraich coordinate systems are not identical, though linear transformation can be used to move from one coordinate space to the other. The basic principles underlie spatial normalization are described based on Ashburner and Friston (1999; 2003b).

Two approaches can be used to register images to a standardized space: label based and intensity based. *Label-based techniques* identify homologous features in the source and reference images and find the transformation that best superposes them. The homologous features are usually identified manually. The problems with this technique are that it is subjective, it is hard to find reliable labels in the brain, and though the transformation of the labels is clear it gives no estimation on how to transform non-labelled regions. *Intensity-based techniques* identify spatial transformations that optimize voxel-similarity measures between a source and a reference image, where both are treated as unlabelled continuous processes. The

matching criterion is based upon minimizing the differences between the two images. The criterion for matching is reached when the reference image appears like a warped version of the source image i.e. when grey levels in the source and the reference images correspond to each other. The latter technique is the one adopted by SPM2.

The first step in image normalization consists of a set of affine transformations i.e. transformations that preserve spatial relations within an image (i.e. parallel lines will still be parallel after an affine transformation). These transformations are based on 12 parameters: six for positioning the brain in the coordinate space and six relating to zooms and shears transformations. The former uses rigid-body transformation methods and the latter parameters are for resizing, stretching and/or compressing the brain.

The criterion for a best match between source and reference is determined using a Bayesian framework. A solution (the best fit set of transformations) is reached by maximizing the a-posteriori probability (the probability of the data given the parameters). This is achieved by iterative procedures that maximize the product of the likelihood function (the probability of the parameters given the data) and by restraining it with prior functions (the probability of the parameters). The Bayesian framework enables SPM2 to incorporate into the warping model a-priori probability regarding the distribution of the data, to increase efficiency and validity of the deformation field. Example of the a-priories used for the affine transformation is the distribution of healthy subjects' head size and shape.

However, human brains differ not just in their size and overall shape but also in the form of their inner structures (e.g. shape of ventricles, gyri). A given voxel can anatomically be localized in different brain structures for different subjects. For example, a voxel localized to the amygdala in one subject can be localized to the hippocampus in another. To accommodate for these anatomical differences between subjects nonlinear warping methods are used. SPM2 models the signal at each voxel as linear combinations of three dimensional discrete cosine functions. By default, 117 parameters are used to estimate each deformation field in the three orthogonal directions. These parameters are computed iteratively to minimize the sum of

squared differences between the images and the template. Again using Bayesian framework, a-priori knowledge is used to optimize the procedure, such as the expected distribution of grey matter, white matter and CSF in the brain.

#### **2.4.1d Spatial smoothing**

Smoothing is done by convolving a Gaussian kernel function with a known full-half-maximum-width (FHMW) to the image. In all studies reported here, the voxel size was 3\*3\*3mm and data was smoothed using a 9mm FHMW of Gaussian kernel. There are several reasons for smoothing fMRI data. The first relates to the assumption of anatomical-functional relation, though this assumption is likely to hold scale (i.e. face selective voxels are likely to be found in right fusiform gyrus of right handed healthy subjects), there is still quite a lot of variability between subjects in specific function locations in the order of tens of millimetres (for variability in face area location, see Kanwisher et al., 1997). This variability was also demonstrated using cytoarchitectonic maps, for example, the anatomical localization of the striate cortex (V1) along the calcarine sulcus between humans was shown to vary (Gilissen and Zilles, 1996). When considering associative cortices, the variability of functional-anatomy relations across subjects increases (Amunts et al., 1999). In all the studies reported here voxel comparisons were made across subjects and therefore smoothing was applied to minimize spatial-function variability between subjects'.

The second reason for smoothing relates to the statistical test used for inferences i.e. the random field theory, where the data is assumed to be continuous and not discrete (Brett et al., 2003). Smoothing shapes the data to have a more continuous structure.

#### **2.4.2 The general linear model**

Statistical analysis of the fMRI data is realised using the general linear model and is described, based on Keibel and Holmes (2003). The general linear model describes the observed data, based on a linear combination of a-priori defined factors and an error term, such that a given  $\mathbf{Y}$  data point is described as the sum of a set of variables  $\mathbf{x}_{(1...m)}$  (i.e. the design matrix) that are differently weighted  $\boldsymbol{\beta}$  (i.e. the parameters) and an error term  $\epsilon$ . The error terms describe the residual variability in the data that the model cannot explain.



$$Y_1 = x_{11} \beta_1 + x_{12} \beta_2 + x_{13} \beta_3 \dots + x_{1m} \beta_m + \varepsilon_1$$

A linear description is generated for each data point. In the case of fMRI, a data point is a voxel and its intensity changes with time. The set of variables i.e. the design matrix is identical for all voxels. The different weighting parameters are estimated separately for each voxel to best fit the data, thus generating different estimates at each voxel for a given model.

#### 2.4.2a Design matrix and contrasts

The design matrix is a set of pre-defined variables, which are termed regressors. Linear combinations of the regressors span the space of possible fMRI responses for a given experiment, up to the level of error. As we are dealing with several regressors for which an estimator should be derived (i.e.  $\beta$ ) it is more efficient to use matrix methods to solve these equations mathematically. Hence:

$$Y = X \beta + \varepsilon$$

Where  $Y$  is a vector representing the time series for a given voxel,  $X$  the design matrix with columns for each explanatory variable (i.e. regressor) and rows for each time point,  $\beta$  is a vector representing the different estimated weighting for each regressor such that a combination of them will best fit the observed data.  $\varepsilon$  is a vector describing the error for each data point, i.e. the remaining variability that could not be explained by the model. The  $\beta$ s are the unknown variables. The number of  $\beta$ s (corresponding to the number of explanatory variables) is usually smaller than the number of observations (i.e. time points) therefore the value of  $\beta$ s can only be estimated. This estimation can be done by minimizing the residual sum of squares between the actual observed data and the fitted data (i.e. the linear combination of the explanatory variables) or by minimizing the error by estimating the likelihood probability, as done by SPM2. It should be noted that although the  $\beta$ s are estimated to best fit the observed data, statistical tests should still be applied to assess the significance of the model before inferences can be drawn.

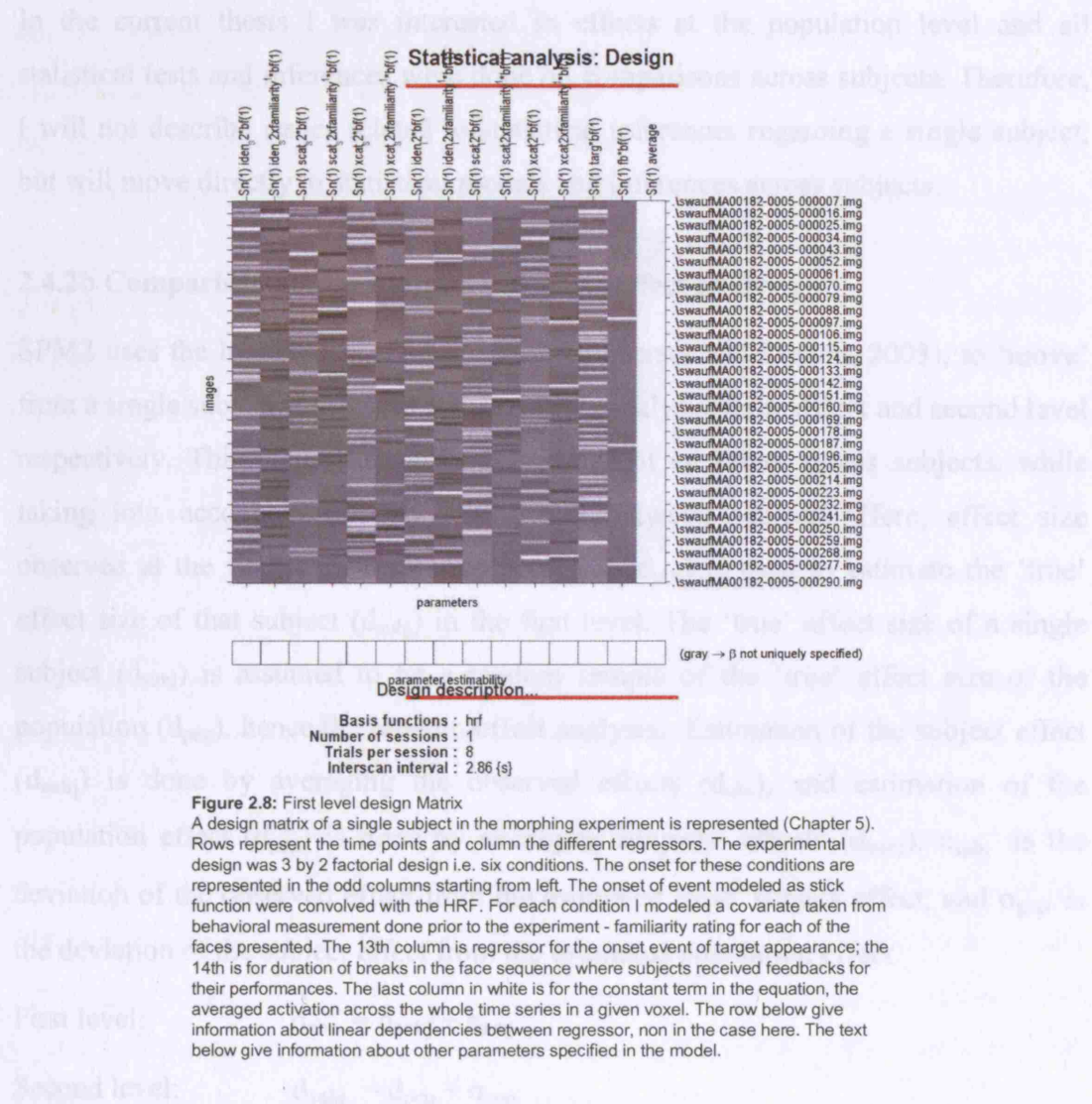
The design matrix includes all possible variables that could potentially explain the observed data. To avoid an over-determined model that leads to an infinite number of solutions, variables which are linearly dependent should not be used. An example of a design matrix, used in the experiment reported in Chapter 6 is presented in **Figure**

**2.8.** The design matrix is a graphic description of the expected ‘behaviour’ of the time series where white denotes expected high intensity and black expected low intensity signal. The rows represent different time points measured in scan volumes and the columns are the explanatory variables. Typically each condition is reflected by one regressor, where high intensities are expected when this condition occurred i.e. depicting the onset and duration of trials for this specific condition.

As discussed in section 2.3, the BOLD reflects a haemodynamic response, and the shape of this is shown to be reliably described by using two gamma functions. It is termed the canonical ‘haemodynamic response function’ (HRF, Friston et al., 2003). To accommodate for such a response function the regressors are convolved with the canonical HRF. It should be noted that there are other methods to characterize the haemodynamic response (HR), some which allow greater flexibility in describing the shape of the response (e.g. a flexible basis set), or adding regressors to capture variability in the onset and width of the HRF. In the current thesis inferences were only done at the population level where the canonical HRF was assumed to be sufficient for capturing changes in the BOLD response corresponding to the different conditions.

The model that is specified in the design matrix should include any information that is likely to affect the recorded MR signal. This is done to reduce the error term (the unexplained data) in the model, as the smaller the error term the higher is the sensitivity of the statistical tests. The design matrix reported in **Figure 2.8** for example, includes regressors that depict the onset and duration of the experimental conditions. For each condition an additional regressor was added that describes a parametric modulation of the response to that condition, namely the familiarity rating of the faces in each trial. Two additional regressors of no interest were added to the model one for the targets and another for the feedback events. In the experiment described in **Chapter 5** parameters from the rigid body transformation were entered to the design matrix to control for effects that are due to head movements. This was not done in the other experiments, as the unwrapping procedure corrects for these possible artefacts in the time series. SPM2 automatically assigns additional regressors to the design: a regressor with a constant value depicting the average signal intensity along the whole session and a set of low frequency cosine functions

with harmonic periods, used as high pass filters. The latter are used to explain any low frequencies changes in the time series, such as drifts.



**Figure 2.8:** First level design Matrix

A design matrix of a single subject in the morphing experiment is represented (Chapter 5). Rows represent the time points and column the different regressors. The experimental design was 3 by 2 factorial design i.e. six conditions. The onset for these conditions are represented in the odd columns starting from left. The onset of event modeled as stick function were convolved with the HRF. For each condition I modeled a covariate taken from behavioral measurement done prior to the experiment - familiarity rating for each of the faces presented. The 13th column is regressor for the onset event of target appearance; the 14th is for duration of breaks in the face sequence where subjects received feedbacks for their performances. The last column in white is for the constant term in the equation, the averaged activation across the whole time series in a given voxel. The row below give information about linear dependencies between regressor, non in the case here. The text below give information about other parameters specified in the model.

In fMRI studies, differential effects are mainly tested, i.e. comparisons between conditions. Differential effects are calculated using contrasts (Poline et al., 2003). A contrast is a weighted summation of the different parameter estimates. For example for the design matrix in **Figure 2.8** the contrasts  $[1 \ 0 \ -1 \ 0 \dots]$  computes new linear combinations of the parameters estimates that describe the differential effect size (d) between two conditions in each voxel.

$$d_{(\text{subj})} = (1) * \beta_{(\text{within})} + (0) * \beta_{(\text{famCov-within})} + (1) * \beta_{(\text{identical})} + (0) * \beta_{(\text{famCov-between})} \dots$$

The differences are saved as an image and later serve as the data in a second level analysis, described next.

In the current thesis I was interested in effects at the population level and all statistical tests and inferences were done on comparisons across subjects. Therefore, I will not describe issues related to statistical inferences regarding a single subject, but will move directly to statistical models and inferences across subjects.

#### **2.4.2b Comparison across subjects - random effect analysis**

SPM2 uses the hierarchical models approach (Penny and Friston, 2003), to ‘move’ from a single subject analysis to across subject analysis, termed first and second level respectively. This method tests for robustness of an effect across subjects, while taking into account variability within and between subjects. Here, effect size observed at the first level for a single subject ( $d_{obs}$ ) is used to estimate the ‘true’ effect size of that subject ( $d_{subj}$ ) in the first level. The ‘true’ effect size of a single subject ( $d_{subj}$ ) is assumed to be a random sample of the ‘true’ effect size of the population ( $d_{pop}$ ), hence the random effect analysis. Estimation of the subject effect ( $d_{subj}$ ) is done by averaging the observed effects ( $d_{obs}$ ), and estimation of the population effect ( $d_{pop}$ ) is done by averaging subjects’ effects ( $d_{subj}$ ).  $\epsilon_{subj}$  is the deviation of the observed effect from the estimated ‘true’ subject effect, and  $\sigma_{pop}$  is the deviation of the subject effect from the estimated population effect.

First level:  $d_{obs} = d_{subj} + \epsilon_{subj}$

Second level:  $d_{subj} = d_{pop} + \sigma_{pop}$

$$d_{pop} = d_{obs} - (\epsilon_{subj} + \sigma_{pop})$$

Note that estimation of the variance in the second level is based both on the variance brought from the first. The second level thus reflects both the within and between subjects variability (Penny and Friston, 2003). It should be noted that in fMRI the between subject variability is much larger than the within subject variability, hence the contribution of the latter is smaller in random effect analysis.

### 2.4.2c Classical statistical inferences

The significance of an effect is tested for each voxel using  $t$  or  $F$  -distributions. In the case of one sample  $t$ -tests, the significant of the effect is tested against the null hypothesis that there was no effect, i.e.  $d_{\text{pop}} = 0$ . This is done by dividing the estimated population effect by the square root of its variance. In a similar way, other statistical parametric tests can be used generating different null hypotheses, such as paired  $t$ -test, ANOVA. However, an important assumption for these later tests is that data points (in the case of second level, the parameter estimates) are independent measures. If this assumption is violated the statistical test is invalid. Therefore, when taking more than one contrast from the same subject to the second level, sphericity corrections should be used. fMRI designs are usually in the form of repeated-measurement, therefore when not using a one-sample  $t$ -test, one should also pay attention to the way the error term is defined in the second level, specifically controlling for the overall differences between subjects that are not specific to the tested effect. Most of the inferences reported here were done using a one-sample  $t$ -test in the second level, to avoid the need for sphericity correction.

**Type I error** is a matter of much concern in fMRI analysis, as statistical tests are performed for each voxel separately creating the problem of multiple comparisons. Classical statistical inferences made with confident levels of 95%, have by definition a 5% chance of reporting false positive activations, such that for any given 1000 voxels, we would expect 50 voxels to show above threshold level of activation by chance. This problem is termed family wise error (FWR).

Several solutions have been suggested to protect against false positives. The most conservative is the Bonferroni correction, where the desired confidence level (say 95%,  $P < 0.05$ ) is recalculated by dividing it by the number of comparisons. In the case of the studies reported here, a typical search volume contains about 65 thousands voxels, after the Bonferroni correction the corrected  $p$  value for identifying a true effect with 95% confidence level will be  $P < 0.0000007$ . An alternative approach relies on the nature of imaging data, in which each voxel is not an independent measure (as assumed by the Bonferroni correction), but spatially correlated with its neighbours. These spatial correlations are partly due to the

smoothness and partly to the nature of fMRI data. They are described in units termed 'resels' which divide the image to chunks in a size equivalent to the full-half-maximum-width of the estimated smoothness of the data. Using random field theory, the topographic shape of the statistic maps can be predicted based on the number of resels in the image. Specifically, the likelihood of observing peaks with a certain height or width by chance is known. Random field theory states that the fewer the resels, the less likely it is to observe peaks with a given height and width by chance in an image. Thus, as an image gets smoother, the likelihood of observing a peak by chance decreases. SPM2 uses either Bonferroni or the random field theory to correct for FWR, depending on the actual smoothness of the image.

In all the experiments reported here, there was a clear a-priori hypothesis regarding the anatomical localization of the experimental effects. Therefore a region of interest approach was adopted using a more liberal threshold of  $P < 0.001$  to 0.005 for reporting effects.

**Type II error** (i.e. not detecting an effect that truly exists) could be affected by variance in the data. The smaller the variance (the error term in the model) the more sensitive and powerful is the statistical test to detect an effect. SPM2 works to minimize the error term through all stages, in the pre-processing, the design matrix etc.

## 2.5 EXPERIMENTAL DESIGN

Experimental designs of studies measuring responses using fMRI signal should obey the same research rules as any other cognitive experiments measuring behaviour responses. In addition fMRI experimental designs should take into account the nature of the expected response in order to optimize this measurement. Next I describe specific experimental design issues relevant to the experiments reported here.

Experimental manipulations can be at the level of the stimuli or the task. If stimuli are manipulated, the task should be kept constant and vice-versa. fMRI signal

measurements are sensitive to everything that goes through a subject's head during the experiment, therefore it is very important to make sure the design is optimized. Use of a task that engages a subject's attention and resources is one way to control this. In the experiments reported in chapter 5, 7, 8 and 9 only the stimuli were manipulated and the task was kept constant through out the experiment. Moreover, in these cases the task was unrelated to the experimental manipulation and its role was to make sure subjects attended to the presented stimuli. In the experiment reported in **chapter 6** (i.e. the spatial frequency experiment) the task and the stimuli were both manipulated, and all stimuli were presented twice under both task conditions. In this particular experiment as stimuli were hybrid faces there was a risk that attention would confound the stimuli manipulation. The task was used to direct subjects' attention to one of the other components of hybrid faces.

Manipulation of stimuli alone during fMRI experiments can introduce potential difficulties in interpreting the meaning of the effects observed, as no relevant behavioural responses are collected. Therefore, in the experiments reported in chapters 5, 7, 8 and 9, to validate the experimental manipulation additional off line behavioural experiments were conducted to collect relevant behaviour responses, and these were sometimes used as covariates in the fMRI analysis. Collecting relevant behaviour responses from subjects can also be used to explain variability within and between subjects, as was done in the experiments reported in chapters 5, 7, 8 and 9.

All experiments reported here were designed as event related fMRI. *Event related designs* refer to cases where responses are modelled separately for occurrence of each single event. As discussed earlier the haemodynamic response for a single event peaks after about 6sec and returns to the baseline only after 30sec. Therefore the first event related designs in fMRI used stimuli onset asynchrony (SOA) of about 30sec, to avoid overlapping responses between events. However, it has been shown that the BOLD response, with some constraints, can be described as linear (Boyton et al., 1996; Rees al., 1997; Robson et al. 1998; Logothetis and Wandell, 2004). Such, that a BOLD response for a single stimulus can be used to predict BOLD responses for two stimuli. This is known as the linear time invariant (LTI) assumption. Though it should be noted, these linear relations are very limited, for example a BOLD response for a single stimulus of 1sec cannot reliably predict BOLD responses for

8sec stimuli, and not even for 6sec stimuli (Robson et al., 1998). It was also shown that this linearity does not hold for short SOAs (Boyton et al., 1996; Ress et al., 1997), or for short/long stimuli duration (Rees et al., 1997). In all these cases the observed response is smaller than what would be predicted. SPM2 relies on the LTI assumption and linearly convolves the canonical HRF of the stimulus onset function to predict the BOLD response. In order to avoid violating this assumption, the SOA should not be shorter than 1sec, and between conditions SOA and number of consecutive events from the same condition should be equalized.

The relation between the sampling rate of the data acquisition (i.e. the TR) and the SOA determines the effective sampling rate of a response, and is specifically important in cases of event related designs. Increases in the effective sampling rate can be achieved by allowing the signal sampled at any given voxel to reflect different time points along the HRF response. This can be done by ‘jittering’ the SOA in respect to the TR, such that the SOA is not a simple multiplication of the TR. In addition assuring a non fixed relation between the TR and SOA protects one from confounding sampling rate with anatomical location. In the experiments reported in **Chapters 5**, and **7** jittering was implemented using ‘null events’. In experiments reported in **Chapters 6, 8** and **9** the SOA was made to be different than TR.

‘**Null events**’ are events that appear randomly along the course of the experiment, where no stimuli are presented and are usually implemented by extending the presentation duration of the fixation point that is presented between events. In the case of visual stimulation the use of null events allows the signal in sensory and associative cortices to saturate, as no input is presented. Null events were used in the experiments reported in **Chapters 5** and **7**.

**An fMRI repetition-related decreases** design, termed fMR-adaptation (Grill-Spector and Malach, 2001) was used in three of the experiments reported here (**Chapters 5, 6** and **7**). This is a specific fMRI experimental design that relies on the observation that stimulus-specific decreases can be observed in the BOLD response following repetition of that stimulus (Grill Spector et al., 1999). As this repetition is stimulus specific it is assumed to reflect underlying neuronal changes in activation and not an overall saturation of the BOLD signal due to repeated presentations. An



alternative way of explaining this phenomenon is by looking at the other side of the same coin, i.e. increase activation following a specific change as a marker for region sensitivity.

There are several advantages to using such design for fMRI studies. One is that it can increase the spatial resolution of the fMRI by enabling one to detect the sub-voxel neuronal sensitivity to different aspects in the stimuli. The rationale is that if a voxel shows a decrease in signal following repetition of one aspect of the stimulus but not for other, this voxel reflects activity of neurons that represent the first aspect of the stimulus and not the other. Another advantage of the repetition-related decrease paradigm is that one controls for all differences in visual attributes of stimuli, as the same stimuli can be used in different repetition contexts.

A possible disadvantage for using repetition-related paradigms is that attention might confound the interpretation with reduced activity reflecting subjects being less attentive due to stimulus repetition than when it changes. To avoid such attention confounds, in all reported experiments the task that was given to the subjects was orthogonal to the repetition paradigm, and an additional set of stimuli were used as fillers to hide the repetition structure of the design. Another disadvantage is that it relies on the assumption that neurons decrease their signal for a repeated presentation of a stimulus, as this assumption might be valid only for some brain regions and not for all.

# CHAPTER 3:

## ELECTROENCEPHALOGRAPH

## IMAGING

---

### 3.1 INTRODUCTION

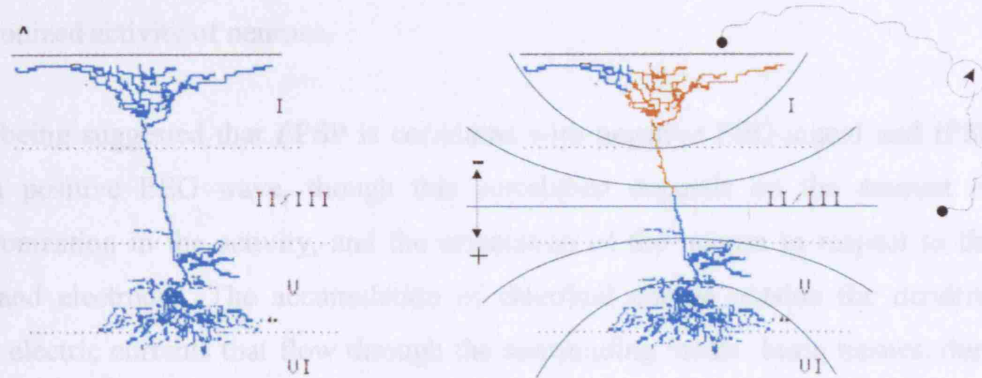
The first person to observe electrical current change on the surface of the brain was Caton (1875). He, and others, demonstrated that electroencephalogram (EEG) currents change due to spontaneous activity and to evoked responses by an external stimulus. Berger (1929) was the first to record EEG signals from humans, using electrodes that were placed directly on the epidural surface of post neurosurgery patients. He was followed by Adrian and Matthews (1934) who recorded EEG from the scalp, and hence opened the way for the use of EEG recording with healthy volunteers.

I start by describing the current opinions regarding the source of the electric current recorded in scalp electrodes, followed by a brief description of the technical side of the method that was used for EEG recordings. In section 3.4, I discuss the advantages and disadvantages in using EEG for cognitive neuroscience research. The EEG experiment that is reported in **Part IV** was analysed using SPM\_EEG developed in the Wellcome Department for Imaging Neuroscience, UCL and will be described in section 3.5.

### 3.2 THE SOURCE OF SCALP ELECTRONIC CURRENTS

The flow of information within and between neurons is conveyed by electrical and chemical changes. At rest the membrane potential is  $\sim 65\text{mV}$ , being more negatively charged inside the neuron. This electric potential is described as the neuron steady-state. Changes to the steady state potential can be triggered chemically or

electrically. A local change in the membrane potential generates an electrical current. Such that when a membrane potential becomes less polarized locally (less negatively charged) an electric gradient is created along the whole cell membrane since other parts maintain their steady-state polarization. This electric gradient leads to flows of ions within the cell and outside the cell to compensate for the gradient (**Fig. 3.1**).



**Figure 3.1 Electrical currents in the cortex**

**A.** In pyramidal neuron the dendrite tree originate in the most superficial layer of the cortex. It has an apical main dendrite that convey the information to the cell body which is located usually in deeper cortical layers. The steady state membrane potential is negative -65mV. **B.** Depolarization of the dendrite's membrane following post synaptic activation generates an electric potential between the dendrite's tree and the cell body. This potential could be measured from the scalp, where the maximum potential would when the electrode is place perpendicular to the apical dendrite. Blue - polarized membrane. Orange -depolarize membrane. Green – the equipotential lines, describing the electric filed.

Membrane potential changes can happen at any part of the neuron: in the dendrites, the soma or the axons. Changes in the axon's membrane potential are associated with action potentials. Changes in the dendrite's membrane potentials are termed post-synaptic potentials. The sum of the post-synaptic potentials determines the net polarization at the starting point of the axon, and when this value passes a given depolarization threshold an action potential is generated. Post-synaptic potentials can be excitatory (i.e. depolarizing) or inhibitory (i.e. hyperpolarizing), EPSP and IPSP respectively. The action potential propagates actively along the axon arriving at its end terminal where it causes a release of chemical substances, which affect the postsynaptic potentials of other neurons.

The EEG signal is assumed to be related to electrical changes in post-synaptic potentials rather than action potentials. Post-synaptic potentials last longer (10-250msec) and their electrical charge accumulates over time and inputs. Recall, that the BOLD contrast (in fMRI) is associated with local field potentials (LFP's) arising from post-synaptic activity. However, an important difference might be that the BOLD, as opposed to the EEG, reflects metabolic processes and hence does not depend on synchronized activity, whereas EEG signal is assumed to rise from synchronized activity of neurons.

It has been suggested that EPSP is correlated with negative EEG signal and IPSP with a positive EEG wave, though this correlation depends on the amount of synchronization in the activity, and the orientation of the neuron in respect to the scalp and electrodes. The accumulation of electrical charge outside the dendrite causes electric currents that flow through the surrounding media: brain tissues, dura matter, cerebral spinal fluid, skull and skin. The electrical currents change the electrical potential on the scalp by Ohm's law due to the electrical resistance of the tissues. This is why recording EEG signals from the scalp or from the cortex surface differs in the extent of the spatial distributions they reflect and the amplitude of the recorded signal. An intracranial EEG signal source is more closely linked to the site of the electrode, while scalp EEG signal is a result of summations over large brain regional activations.

The effect a post-synaptic potential change (i.e. the source) will have on the scalp's potential depends on its depth, orientation and structure. As the distance between the source and the recording site (i.e. the scalp) increases the amplitude of EEG signal decreases. On the other hand conductivity across the brain is not uniform, with CSF having the lowest impedance compared to grey matter and white matter being the least conductive. Thus a deep structure in vicinity to CSF, such as the brain stem, will be more likely to affect the scalp potential than a deep structure surrounded by white matter such as the putamen. The orientation of the dendrites generating the source in respect to the electrode, also affect the EEG signal. EEG signal amplitude will be higher when recorded perpendicular to the axis of the electric gradient (i.e. the dipole). The structure of the neurons dendrites affects the overall summation of the current flow, such that when neurons are organized in a symmetrical way they

generate opposite electric currents which cancel each other. Note, that in the EEG's forward model, which describes the relation between neuronal activity and its manifestation on the scalp, the electrical signal is very complex, posing an additional computational problem on the inverse solution (determining the source of activity based on the scalp electrical response).

Given the above, the best candidates for generating the EEG signal are the dendrites of the pyramidal cells. These are the most common cells in the cortex, and their dendritic trees usually originate in the superficial layer of the cortex closest to the scalp, with the apical dendrite (the main branch) oriented perpendicular to the surface of the cortex (**Figure 3.1**).

### **3.3 DATA ACQUISITION – EEG**

Scalp EEG measures electrical changes that are associated with brain electrical activity. These changes are recorded from electrodes that are placed on the scalp and provide a non-invasive technique to evaluate the activity of the human brain during different mental states and in response to stimuli. In the EEG study reported here the data was acquired using the NeuroScan V4.0 system.

#### ***3.3.1 Electrodes***

Electrodes are used to make the connection between the conduction fluid of the tissue in which electrical activity is generated and the input circuit of the amplifier. Electrodes always involve a metal–fluid conjunction. For accurate recording there should be no distortion of the signal at this interface. When an electrode is immersed in an electrolyte, an electron exchange occurs, which causes metal ions to enter into the solution and this exchange causes the electrode potential. Such factors vary with the type of metal. Silver electrodes coated with chloride are the most sensitive and stable electrodes. The conducting medium that was used in the experiment reported here was highly concentrated sodium chloride with the electrode impedance adjusted to be below 5k $\Omega$ .

### 3.3.2 Reference

Detection of electrical signal is done by an amplifier. An amplifier by definition detects a potential difference between two points. The question is then what should be the reference and where should it be located? This is an important issue as the amplifier compares the differences in potentials between recording sites and the reference, hence if both potentials are influenced by a common electrical neuronal activity it will be cancelled out and will not be detected by the amplifier.

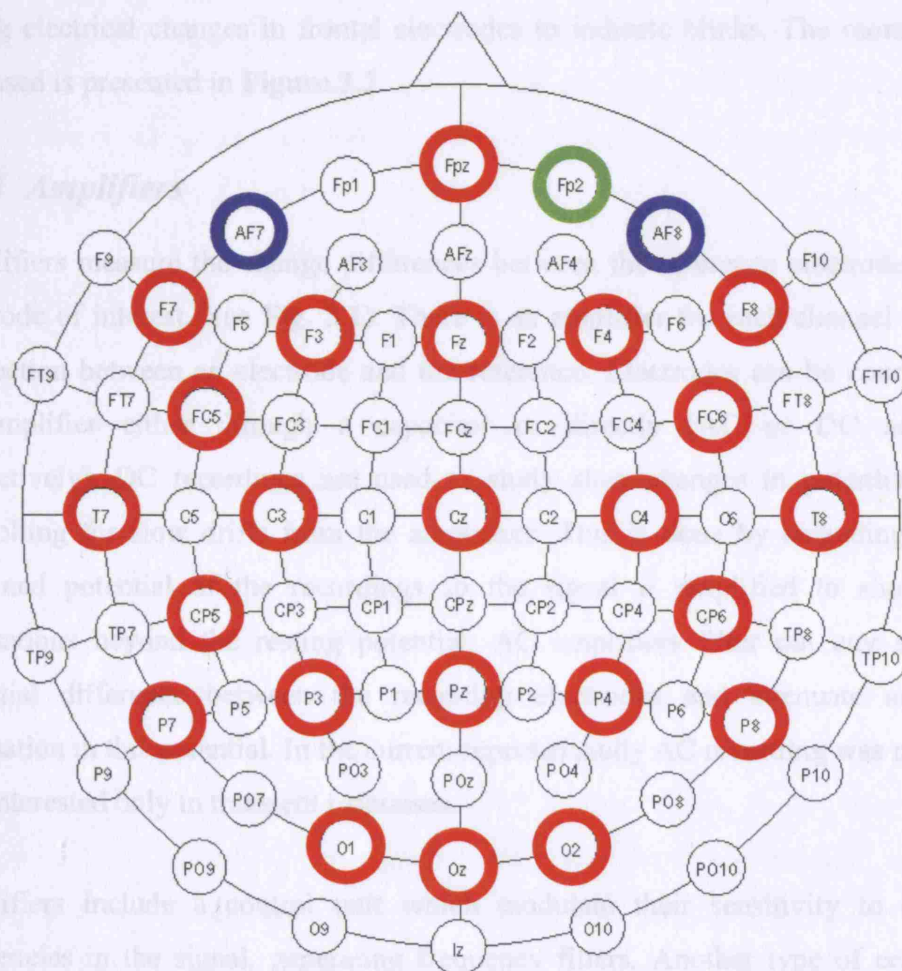
Three possible methods have been suggested for selecting a reference: *bipolar*, a *common reference* or an *averaged reference*. In the *bipolar method* each channel (amplifier) is connected between two electrodes, both of which are likely to be affected by appreciable EEG potentials, generating a serial link between the electrodes. One disadvantage of this method is that one loses a lot of signal, especially in cases where the electrode response is highly correlated. In the *common reference method*, all electrodes are connected through the same electrode/s, thus subtracting the same constant from all. Here, the location of the reference electrode/s is very important as it affects the signal recorded and will differ depending on the distance of the reference from the electrodes. Therefore, the reference is usually placed as far as possible from the site of expected effects. The third method that is suggested is to use the *averaged signal* from all electrodes as a reference, this is usually done offline. This last measure of the reference must be based on adequate sampling from all surfaces of the brain, including neck, face and lower scalp parts.

In the current experiment I used the *common reference method* with the ears-linked serving as the reference electrodes, by combining activity from both ears. Using the ears-linked as references was done for several reasons: 1) two ears served as reference to avoid laterality biases that could occur in the case of reference from a single ear; 2) the number of total electrodes used (27) was inadequate for reliable measure of the averaged signal from all electrodes. Finally the design of the experiment replicated a previous experiment which uses ears-link as references (Eimer and Holmes, 2002). Ears-link pick up signal from the base of the brain, hence this signal could not be optimally measured in this experiment.



### 3.3.3 Recording montage

Simultaneous recording from multiple scalp electrodes are essential for understanding EEG and ERP in particular. To allow comparisons between labs and different subjects the location of the electrodes on the scalp is determined, based on uniform marking space. This space is called the “Ten-Twenty” system (Jasper, 1958). To accommodate for subjects different head shape and size, electrodes are placed based on calculated percentage distances from the central electrode (i.e. Cz). The location of the Cz on the scalp, is determined as being equally distance from theinion and nasion, and from both ears.



**Figure 3.2** The 10-20 montage

Marked in circles are the electrodes used in the experiment reported in Part IV, Data was recorded from the red electrodes (total of 24), green was the ground and the blue electrodes recorded horizontal eye movements.

The montage specifies any additional electrodes that can be use for artefact reductions, such as an electrode that is connected to the ground. The use of this electrode is important and serves as a large sponge for accumulated charge. This connection to ground drains off charge that may develop in subject's scalp through capacitive inductance from power lines or other sources of high voltage. In addition a ground electrode improves signal-to-noise. Horizontal and vertical electro-oculogram (HEOG, VEOG, respectively) can be place around the eyes to record eye movements and blinks. Eye movements generate strong positive electrical change which is much larger than the ERP signal. Hence, information regarding eye movements can be used to correct for this artefacts off line or as indication of trials that should be omitted from the analysis. In the study reported here I used only HEOG and relied on strong electrical changes in frontal electrodes to indicate blinks. The montage that was used is presented in **Figure 3.2**.

### ***3.3.4 Amplifiers***

Amplifiers measure the change differences between the reference electrode and the electrode of interest (See **Fig. 3.1**). There is an amplifier for each channel i.e. each connection between an electrode and the reference. Electrodes can be connected to an amplifier either through a capacitor or directly (AC or DC amplifiers respectively). DC recordings are used to study slow changes in potentials while controlling for slow drifts from the amplifiers. This is done by balancing out the sustained potential of the recordings so the signal is amplified to show small fluctuations beyond the resting potential. AC amplifiers filter out any sustained potential difference between the recording electrodes and attenuate any slow fluctuation in this potential. In the current reported study AC recording was used, as I was interested only in transient responses.

Amplifiers include a control unit which modulate their sensitivity to different frequencies in the signal, generating frequency filters. Another type of commonly used filter is a notch filter, which is used to eliminate 50-60Hz frequency interference. In the study reported here a notch filter was used, as a 50Hz noise was observed in the recording system.



Once amplified, the analogue signal is converted into digital form for computational processing. The conversion is done based on a-priori determined sampling rate. The sampling rate must be more than the Nyquist rate, which is twice the highest frequency presented in the signal. In the case of the study reported here the sampling rate was 200Hz.

### **3.4 USING EEG FOR COGNITIVE NEUROSCIENCE**

#### **RESEARCH: PROS AND CONS**

EEG is a commonly used tool to measure brain response in humans. A typical experiment involves recording changes in brain potential to different stimuli under various task demands. In the following paragraph I describe the pros and cons of this technique by comparing it to other available tools in neuroscience.

##### ***3.4.1 Safety issues***

EEG is a non-invasive technique. However, faulty equipment and an 'unclean' electrical environment can be health hazards. Two types of risks can occur. One is the possibility of spark ignition of explosive anaesthetic mixture therefore such substances should be avoided in the vicinity of an EEG recording system. Second, there is the risk of passage of electrical currents through the volunteer's body. This problem is called leakage current and can cause pain, burns, respiratory arrest etc. Leakage current can occur if there is an insulation breakdown that causes electrodes to carry high voltage. A disconnection between the ground electrode and earth can have similar effect. To avoid an uncontrolled increase in electrical voltage in the vicinity of the subject it is recommended to create an isolated electronic environment, specifically not to use electronic devices connected to the main power but rather use batteries for the electronic supply. An isolated electronic environment also improves signal noise.

### ***3.4.2 Spatial resolution***

Spatial resolution is a major draw back of EEG scalp recordings, as there is no simple way to relate the location of electrodes to specific brain regions. This is a type of inverse problem where transformation of spatial information from 2D to a 3D space is required. As described above, in the case of EEG the forward model is also not trivial, which makes the inverse problem harder to solve. As in most inverse problems, this problem cannot be resolved unless constraints are introduced to the possible solutions. To date, there is no reliable method that is accepted across labs for solving the inverse problem therefore it is very speculative to describe EEG in terms of spatial resolution. Due to the lack of spatial information it is difficult to compare EEG results with other research modalities in neuroscience, thus limiting the scientific discourse within the EEG modality.

### ***3.4.3 Temporal resolution***

ERP's biggest advantage is its high temporal resolution, in the order of milliseconds. This allows one to describe sequential processes, and to make inferences regarding the order of their occurrence. This cannot be done using fMRI, as the HRF smoothes out all differential effects in the time domains. However, due to the lack of spatial information EEG cannot dissociate between processes that occur in parallel but only between processes that occur sequentially. Therefore it is biased towards mainly identifying sequential processes.

### ***3.4.4 Understanding the signal***

It is mostly agreed that EEG reflects post-synaptic activity (i.e. the input to a region), similar to fMRI. However it is difficult to interpret the meaning of the signal. For example, does a more negative scalp potential reflect excitatory or inhibitory activation? ERP studies are also restricted to differential effects. But even changes in amplitude in a given time point are hard to make sense of beyond the EEG world, i.e. what does it mean that after 170msec, face stimuli elicit more negative potential compared to objects? Does it mean that 170msec post-stimuli, brain responses are stronger to faces than other objects, or does it mean that after 170msec, brain potentials are more/less in synchronization for faces compared to objects, or maybe it

reflects difference in the spatial distribution of activity etc. Thus one can only speak about differences and the time window at which they occur.

### **3.5 DATA ANALYSIS – EEG**

Once acquired and digitized the EEG data is ready for offline analysis. Analysis includes pre-processing of the data to improve signal to noise and effects of interest are tested using classical statistics. The data reported here was analyzed using SPM-EEG (Keibel and Friston, Wellcome Department, UCL). The principles of this analysis are described next, based on Kiebel and Friston (2004a, b) focusing on the parts of the software that were used in the experiments reported in **Part IV**.

#### ***3.5.1 Signal pre-processing***

The first step in SPM\_EEG is to divide the time series of the EEG to epochs based on the experimental conditions. This is done by defining a time window around the onset of an event that usually starts ~100msec prior to an event onset. Its total length depends on the time window where effects of interest are expected to occur and on the experimental design. In the experiments reported here (Part IV) an epoch length was set to 700msec.

The second pre-processing step is termed baseline correction. The average signal of the pre-stimuli duration is subtracted from the whole epoch, scaling all conditions starting potential to zero. To increase signal to noise, artefacts are removed from the data, using a pre-defined threshold. Epochs that show potentials that fluctuate more than the threshold are discarded. The threshold is determined based on the expected effect size. In the study reported here it was  $\pm 100\text{mV}$ . This threshold also removes epochs where eye movements, blinks or any other facial muscle movements occur, as these result in much larger potential changes than the threshold specified and the ERP expected. It is possible to introduce correction for blinks and eye movements, using a general linear model that estimates the differential effect they have on the different electrodes, but it was not used here.

SPM\_EEG offers a unique solution to estimate the spatial distribution of the signal. This is done using 2D interpolation method. The value of each voxel in a 2D brain is estimated using S-spline basis functions based on its neighbouring electrodes (Kiebel and Friston, 2004a). This allows the use of images as row data to generate SPMs. An important thing to note about this interpolation method is that it might estimate larger responses for pixels between electrodes than the pixel where the electrode is located, as it is not a simple linear interpolation.

### ***3.5.2 Event related potential analysis***

Event related potential, or evoked response potential (ERP) is a specific approach to analyse and understand EEG signals. The basic idea is that electrical activity change in the brain is triggered by an external stimulation or by an internal process. Therefore a given change can be reliably associated to a specific trigger. These changes are usually identified by their peaks and defined based on the peak latency (from event onset), the sign of the potential (positive or negative) and the peak amplitude. ERPs are analysed along the time domain. An alternative approach is to identify the electrical changes following each event based on their different frequencies component. The data reported here was analysed using the ERP approach.

#### **3.5.2a First level, single subject analysis**

Similar to SPM for fMRI, SPM for EEG uses the general linear model as a statistical platform to quantitative evaluation of the data. In the first level analysis a model is generated based on the experimental design and a-priori knowledge regarding the signal for each subject. Similar to the fMRI in an ERP study a design matrix is specified to include all variables that are assumed to have an effect on the ERP signal. The crucial difference is that to date, ERP, as opposed to fMRI response is not well characterized, thus there is no prior knowledge regarding the expected shape of response or of noise that could be generalized over different types of triggers (such as the HRF for fMRI). The response structure along the time domain is much more complex in ERP and varies between electrodes making it even harder to generate a general description. To allow maximum flexibility regarding the shape of the response, SPM for EEG models use time as a factor in addition to the

experimental conditions, such that for any given time point along the epoch the effect size per condition is calculated. In other words the effect size ( $\beta$ ) is the signal amplitude at each time point in each pixel, and its variance is the deviation of each single response from the averaged response.

Contrasts are calculated on a-priori time windows, where the effect size is averaged across these time windows. Differential effect maps are calculated by subtracting averages of different conditions. Results are presented in 2D maps.

### **3.5.2b Second level, group analysis**

As this thesis focuses on inferences at the population level the differential effects are compared across subjects in a similar way to the random effects analysis used for fMRI data. The calculated differential effect can be taken to the second level, and statistical tests are performed using the variance between subjects and within subjects, as described in the hierarchical model approach (section 2.3).

Type I error is corrected using either Bonferonni corrections or the random field theory. It should be noted that this correction protects one from the likelihood of discovering activated voxels by chance, and does not correct for multiple comparison that can occur along the time domain, i.e. the likelihood of discovering differences between conditions at any point in time.

## **3.6 EXPERIMENTAL DESIGN**

ERP response for events as opposed to fMRI does not have a simple characteristic shape. Therefore, methods of deconvolution used in fMRI to deduce the response for a single trial cannot be applied to ERP. This means that when one measures an ERP the SOA should be as long as the expected brain response, to avoid a spilt over response from one trial to the next. Thus a typical ERP SOA will be at least around 1sec. In comparison to fMRI, it is not a disadvantage as fMRI SOA cannot go below 1sec, as the linearity assumption breaks down in such a short SOA.

## Part I: Literature review and methodological background

An additional concern for ERP studies is movements of head, facial and eye muscles. These movements generate strong changes in scalp potentials which directly affect the signal measured in EEG. As opposed to fMRI these movement related artefacts cannot be corrected off line, hence special care should be applied when designing experiments and instructing the subjects so these artefacts will be minimized.

## PART II:

# HIERARCHICAL PROCESS

## OF FACIAL IDENTITY

IDENTITIES – BEHAVIOURAL WORK



# CHAPTER 4:

## CATEGORICAL OR CONTINUOUS

## REPRESENTATION OF FACE

## IDENTITIES – BEHAVIOURAL WORK

---

### 4.1 Introduction

Face identity processing is hypothesized to be hierarchical, encompassing at least three steps with each process a different aspect of a viewed face (see **Chapter 1**). The aims of the following studies were to test whether there is evidence for these hypothesised stages and whether they engage different brain structures. Based on the model (Bruce and Young, 1986) described earlier it is hypothesized that the initial stage in face processing (i.e. the first step in the *structural encoding* phase), is view-dependent being highly dependent on physical properties of a face and is ‘blind’ to information such as facial identity, expression etc. Previous research suggests that posterior occipital cortices are involved in generating such representations (de Renzi et al., 1991; Haxby et al., 2000).

A second prediction relates to the next step in the hierarchical process involving the extraction of identity. At this stage an abstract representation (i.e. structural code) of a face that is independent of viewing conditions and physical properties is generated (Bruce and Young, 1986; Haxby et al., 2000). These models also implicitly assume a *categorical* representation of identity, as each identity is represented by only one



structural code. The fusiform gyrus, a more anterior part of the ventral visual stream has been implicated in the representation of face identities (Haxby et al., 2000; Grill-Spector et al., 2004).

The face space model is an alternative approach to describe the nature of identity representation (Valentine, 1991). Here, faces are represented in a multidimensional space, where the dimensions are different physical attributes. Each face is represented as a vector in that space. This model predicts that faces that are physically similar activate a shared network. It follows that identity is represented within *continuous* space rather than a separate identities occupying discrete – thus *categorical*-regions of space (Nosofsky, 1986; Valentine, 1991). To accommodate the ability to recognize identity across different viewing conditions, later developments in face space models suggest that familiar faces are represented by attractor fields (Tanaka et al., 1999). An attractor field is created by warping the face space around a face-vector. Any face that then activates a particular attractor will be recognized as that field's identity. Based on this model, representations of physical properties and identity are encompassed in the same space and therefore are predicted to engage the same neural network.

Empirically, to dissociate between identity and physical properties of a face is problematic. Both of these aspects of a face are highly confounded, as any change in identity involves a change in physical properties. Past attempts at quantifying a physical change between different identities have been problematic. One approach to quantify physical differences across identities operated on the basis of voxel-by-voxel comparisons between images (Grill-Spector et al., 1999). This measure was highly influenced by the location of a face within the visual field: a failing point, high-order visual regions are known to be insensitive to the location of an object in the visual field (Tanaka et al., 1991). Indeed such physical dissimilarity is shown to be ineffective in modulating higher visual regions' responses to faces (Grill-Spector et al., 1999).

A different approach fuelled the attempts of the current experiments to examine identity and physical properties in isolation. Artificial images of faces were generated through using computer algorithms, thus allowing the amount of physical

change in a face to be quantified. Here, I used a morphing algorithm to generate continua of morphed faces that gradually changed in steps of 10% from one identity to another. This method was used in previous studies to investigate processing related to face identity (Beale and Keil, 1995; Campanella et al., 2000). These studies argue that perception and representation of identity are categorical and not continuous. Intriguingly, no study so far using the above method has demonstrated the existence of representation of the physical properties of a face.

In the following chapter, I report seven studies that aim to disentangle physical and identity representation of faces. **Chapter 4** aims to replicate Beale and Keil (1995), as they only used a limited number of morphed continua (i.e. two continua of famous faces and one of unfamiliar). Here, I generated 43 continua between 86 famous faces, and used classification and discrimination tasks to test for categorical and continuous perception of identity (Harnad, 1988). In addition identity discrimination and a similarity tasks were used to test the effect of task on subjects' responses. In **Chapter 5**, I test for different types of face representations using indirect paradigm, namely an immediate repetition was applied in generating both behavioural and fMRI data. The behavioural priming response was measured under two different tasks: familiarity and gender judgement. Finally, the effects of pre-experimental familiarity on the representation and perception of face identity was tested.

## 4.2 IDENTITY CLASSIFICATION TASK

### 4.2.1 *Method*

**Subject.** 20 volunteers (10 female, mean age: 28y range 22-39y) participated. All had normal or corrected vision with no neurological or psychiatric history.

**Stimuli.** The initial stimulus-set was comprised of 86 achromatic portraits of famous people. Using Photoshop 6.0, all faces were resized to 220\*250 pixels. To optimize the subsequent morphing procedure, the faces were paired by matching suitable original faces based on gender and composition of the photograph. I then morphed between faces in each pair using Morpher 3.1 ([www.asahi-net.or.jp](http://www.asahi-net.or.jp)), to generate a

symmetrical continuum of 11 images (morphs) that represented gradual transitions from one original face to the other in steps of 10% (i.e. 0% through to 100%). The morphing required manual delineation of anatomical loci common to the two faces. Approximately 140 loci were delineated per face, including the outline of the face, forehead wrinkles, eyes and eyebrows, orbicularis oculi, nose, zygomaticus muscles and chin (Winston et al., 2003). Examples of three morph continuum are shown in the x-axis of **Figures 4.1 and 4.2**.

**Experimental procedure.** Prior to the experiment, subjects were exposed to the original morphs and were asked to rate their level of familiarity with each face on a scale from 0 – “do not recognize at all” to 3 – “I know this person very well and can even name him or her”. Note that by exposing subjects to the face set (as in the above procedure) we have a-priori strengthened the possibility to observed categorical perception for these faces. We have used this prior exposure since it is suggested that categorical perception depends on knowledge of the category edges (Harnad 1988). The **identity-classification task** followed that described by Beale and Keil (1986). Each continuum was tested separately, starting with presentation of the two original faces (unmorphed faces) together with their names. This presentation was followed by 33 trials (3 presentations of each of the 11 different morphs) presented in random order. Subjects made 2-alternative forced-choice identity responses for each morph. Morphs were presented for 750ms, followed by a fixation point that remained until subject responded.

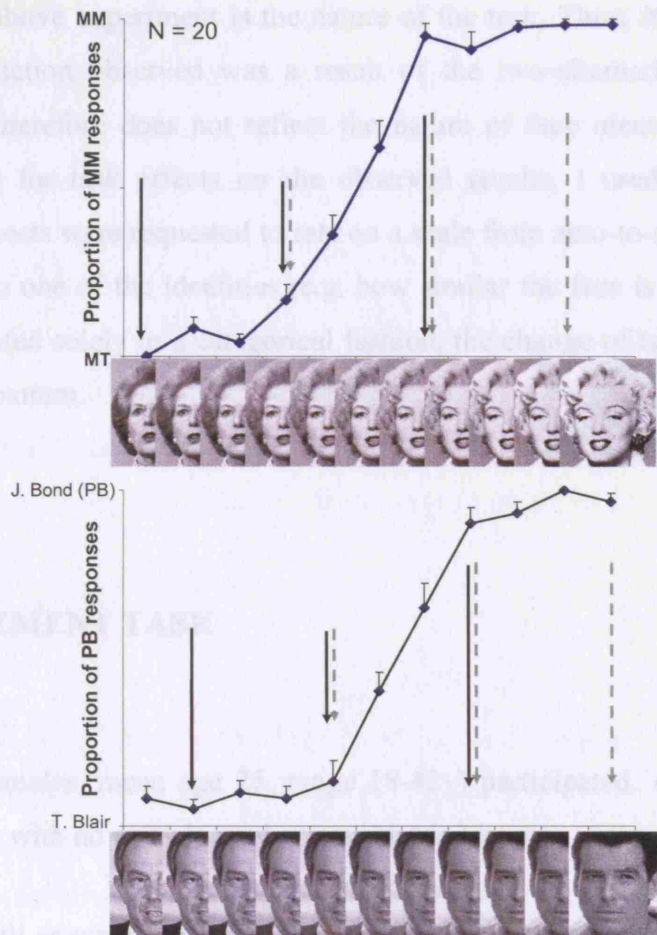
**Analysis.** Parametric characterization of the response function was tested using polynomial regression. To test whether the response function had a continuous or a categorical component, i.e. a step-like function, the parameters estimate for the 2<sup>nd</sup> (linear) and 3<sup>rd</sup> order (sigmoid), averaged across subjects, were tested against zero using a one sample t-test across face-pairs.

### Figure 4.1: Identity classification task

Results of the identity-classification experiment shown for two continua: Top “Maggie-Marilyn”, Bottom: “Blair-Bond”. Along the X-axis the 11 levels of morphs are shown for Maggy & Marilyn / Blair & Bond. The graph represents averaged proportion of responses across 20 subjects in the identity classification task for these continua given for the name shown at top of the Y-axis. MM - Marilyn Monroe; MT - Margaret (Maggie) Thatcher; PB – Pierce Bronsnon (James Bond); TB – Tony Blair. Error bars represented SEM.

The black arrows indicate the three particular morphing levels that constitute the stimuli-set in later experiments. In the top graph, the two levels on the left were reliably identified as MT and the third was reliably identified as MM (i.e. “Maggy-set”). At the bottom the black arrows represent the “Blair-set”. The dash

arrows point to morphs used for another counterbalanced stimuli-set in those experiments, where two of those morphs are now reliably identified as MM, the other as MT (i.e. “Marilyn-set”) or the “Bond-set”.



### 4.2.2 Results & Discussion

An illustrative response profile for two continua is shown in **Figure 4.1**. The response profiles for each face-pair and each subject were fitted by polynomial regression. In addition to a linear component ( $t_{42} = 36.5$ ,  $P < 0.001$ ), a highly significant (negative) cubic component ( $t_{42} = -20$ ,  $P < 0.001$ ) was observed (tested across continua), that captured the step-like (i.e. sigmoidal) function. Such a nonlinear pattern is consistent with categorical perception of identity (Beale and

Keil, 1995). Although the function suggests evidence for continuous representation as well (i.e. the linear component).

One caveat in relation to the above experiment is the nature of the task. Thus, it is possible that the step-like function observed was a result of the two-alternative forced choice task used and therefore does not reflect the nature of face identity representation per se. To test for task effects on the observed results, I used a similarity judgement task. Subjects were requested to rate on a scale from zero-to-six the similarity of each morph to one of the identities (e.g. how similar the face is to Maggie). If identity is represented solely in a categorical fashion, the change of task should not affect the response pattern.

## 4.3 SIMILARITY JUDGEMENT TASK

### 4.3.1 *Methods*

**Subjects.** 39 volunteers (20 females, mean age 25, range 18-42y) participated. All had normal or corrected vision, with no neurological or psychiatric history.

**Stimuli.** The same set of stimuli as were applied in the identity discrimination task, were used here. i.e. 43 morph continua between 86 famous faces.

**Experimental procedure.** Prior to the experiment, subjects rated their familiarity with the faces as above. The 43 continua were divided randomly to 5 blocks of stimuli. Each block was run at a separate session, using different subjects (some subjects participated in more than one session). This was done in order to reduce the load of the task, and minimize fatigue effects. An addition coding for familiarity for name and face was preformed. Here, subjects were presented with the unmorphed faces and names and had to indicate whether they knew the face or not, using a button press. Following this, each continuum was tested separately, starting with the presentation of the target name. The target name could be of either one of identities that was included in the continuum (e.g. rating similarity to Marylin when viewing the “Maggie-Marylin” continuum). A target identity was assigned randomly for each

continuum. Subjects' task was to rate each morph on a similarity scale, ranging from 0-to-6 (0 - 'the face is not the target's face', 1 - 'there is a slight resemblance to the target face' ... 5 - 'the face is very similar but not the target', 6 - 'this is the face of the target name'). This similarity judgement was carried out on the 11 different morphs, each presented 3 times in random order. Morphs were presented for 750ms, followed by the similarity scale that remained until the subject responded. The first continuum in each session (randomly assigned) served as a practice and was excluded from the analysis.

**Analysis.** Parametric characterization of the response function was tested using polynomial regression. To test whether the response function had a categorical or a linear component, the parameter estimates for the 2<sup>nd</sup> (linear) and 3<sup>rd</sup> order (sigmoid) function, averaged across subjects, were tested against zero using a one sample t-test across face-pairs.

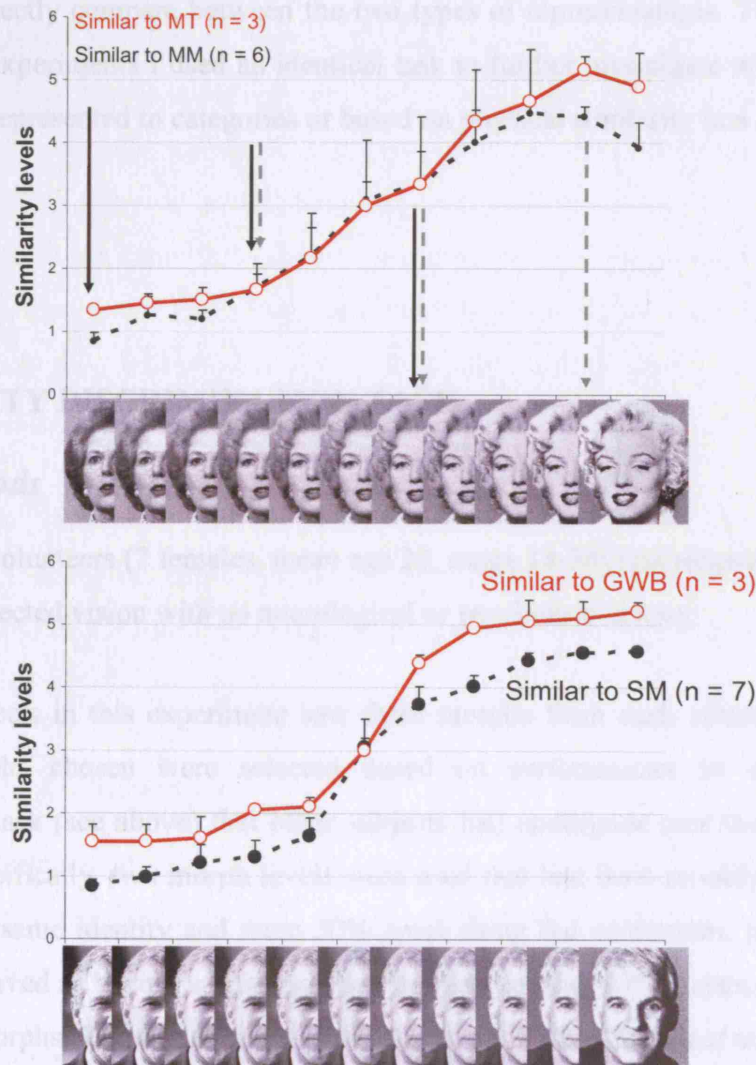
#### **4.3.2 Results & Discussion**

In the *similarity judgement* task, subjects rated the similarity to a particular identity. An illustrative response profile for two continua is shown in **Figures 4.2**. There was no significant difference in the response function that depended on the target identity of each continuum (e.g. whether similarity judgement were done to Maggie or Marilyn, see **Fig. 4.2**). Therefore responses for each continuum were collapsed across target identities. The response profiles for each continuum averaged across subjects were fitted by polynomial regression. A strong linear component, 2<sup>nd</sup> order, was observed ( $t_{42} = 19.26, P < 0.001$ ), as well as (negative) a 3<sup>rd</sup> order component ( $t_{42} = -11, P < 0.001$ ).

A comparison of the response functions between the identity discrimination and similarity judgement tasks revealed that the parameter estimates for the linear component were higher for the similarity task than for the classification task ( $t_{42} = 11.3, P < 0.001$ ). This result suggests that when judging similarity, responses had a greater linear component than when classifying face identity. The opposite pattern was observed for the sigmoid component (i.e. 3<sup>rd</sup> order), where the estimates for the similarity judgement task were lower than for the identity classification task,



indicating a weaker sigmoid component in the similarity judgement compared to the classification task ( $t_{42} = -6$ ,  $P < 0.001$ ). The strong linear component of response observed in the similarity judgement task is inconsistent with the idea that face identity is only perceived categorically (Beale and Keil, 1995).



**Figure 4.2: Similarity Judgement task**

Results are shown for two continua: Top "Maggie-Marilyn", Bottom: "Bush-Martin". Along the X-axis are shown 11 levels from the morph continuum between Maggy & Marilyn / Bush & Martin. The graph represents the average proportion of responses across the subjects who judged similarity for that continuum and are separated depending on the target identity. In black, judgement of similarity to MM - Marilyn Monroe (top) and SM - Steve Martin (bottom); In red: judgement of similarity to MT - Margaret (Maggie) Thatcher (top) and GWB – George W Bush (Bottom). Error bars represented SEM. For comparison with Fig 4.1: The black and dashed arrows indicate the three particular morphing levels used for a stimuli-set in later experiments. Note that here, the categorical boundaries are not clear.

The results of these two experiments suggest that task requirements affect the observed pattern of responses, and therefore interpretation about the nature of representation should be done with caution. They also suggest that both types of representation exist: a continuous representation of physical properties and a categorical representation of identity. However, since I used two different tasks, it is difficult to directly compare between the two types of representations. Therefore in the next two experiments I used an identical task to further investigate whether face identities are represented in categories or based on physical similarity in a continuous fashion.

## 4.4 IDENTITY DISCRIMINATION TASK

### 4.4.1 Methods

**Subjects.** 13 volunteers (7 females, mean age 29, range 18-38y) participated. All had normal or corrected vision with no neurological or psychiatric history.

**Stimuli.** Subjects in this experiment saw three morphs from each continuum. The specific morphs chosen were selected based on performances in an identity classification task (see above) that other subjects had undergone (see the arrows in **Fig. 4.1**). Specifically, two morph levels were used that had been reliably perceived as having the same identity and were 30% apart along the continuum, plus a third that was perceived as having a different identity but was also 30% distance from one of the other morphs. These exemplars were used in the *Within*, *Identical* and *Between* conditions respectively (see below). Two such sets of three morphs were chosen from each continuum (one from each end-point), though any one subject only viewed one of these sets, selected randomly (e.g. either the “Maggie set” – black arrows, or the “Marilyn set” – dashed arrows, **Figs. 4.1**). This meant that, across subjects, the direction of shift along the morph continuum was not confounded with *Within* or *Between* conditions. Note that the faces used in the *Identical* and *Between* conditions were approximately the same distance from an original face (one or other end-point of the continuum); moreover across subjects, these particular face-pairs could appear



(pair-type) by 2(inter-stimulus interval, ISI) factorial design. The three types of pairs were (see **Fig. 4.3a**): *Identical*, where the same image was repeated, with the same physical properties and identity; *Within*, where the morphs came from the same side of identity boundary, but with 30% difference along the continuum; *Between*, where the morphs came from different side of identity boundary and also varied from the first member of the pair by 30% difference along the continuum. Note that the first face in each pair was always the same. Each pair was shown twice, once with a long (500ms) ISI between first and second faces, and once with a short ISI (75ms). Each face was presented for 500ms, with a 2500ms stimuli onset asynchrony (SOA) between pairs. The ISI manipulation was introduced to test whether iconic memory affects subjects' response patterns. The hypothesis was that stronger categorical perception will be observed in the long ISI and physical change effects will be mostly observed in the short ISI. Subjects were instructed to judge whether the two faces have the same or different identities. Subjects were advised that on occasion one identity might be presented with two different pictures. They were asked to respond as quickly and accurately as possible.

**Data analysis.** Data were analysed using Matlab6.0 and SPSS11.0. Results for 'different' responses were represented as a proportion of the total number of pairs per condition (i.e. out of 43\*2). All reported results are Greenhouse-Geisser corrected for violation of sphericity.

#### **4.4.2 Results & Discussion**

Results are presented in **Figure 4.3b**. Participants judgements that stimulus pairs differed depended on their type ( $F_{1.4,13.9} = 80, P < 0.001$ ). As expected, pairs that straddled the categorical boundary (i.e. *Between*) were more often judged as different than *Within* pairs ( $t_{10} = 7.9, P < 0.001$ ). There was also an additional (albeit smaller) effect of physical difference, with *Within* pairs more often judged as different than

## Part II: Hierarchical processes of facial identity

in either of the *Identical* or *Between* conditions in a counterbalanced manner, hence controlling for any effects due to the distance from original faces.

**Experimental procedure.** Prior to the experiment, subjects provided their

in either of the *Identical* or *Between* conditions in a counterbalanced manner, hence controlling for any effects due to the distance from original faces.

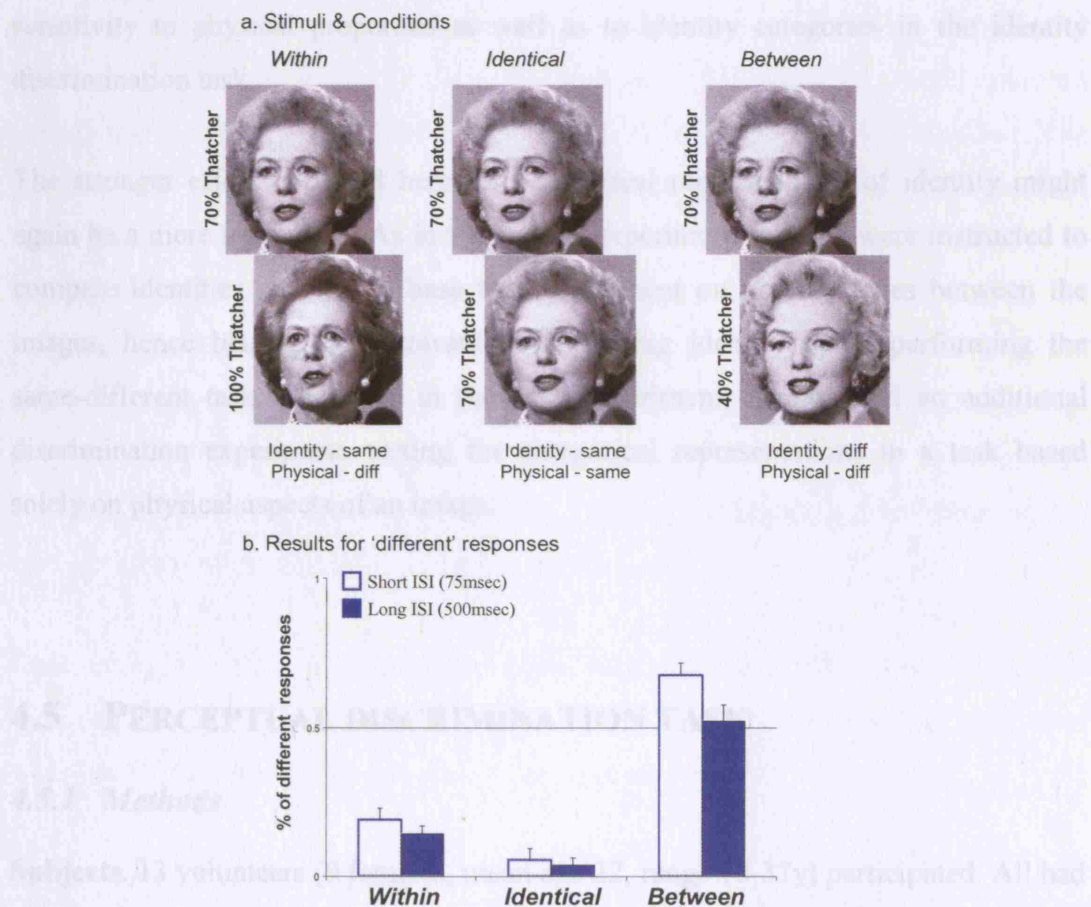
**Experimental procedure.** Prior to the experiment, subjects provided their familiarity rating for each of the famous faces as above. The experiment had a 3 (pair-type) by 2(inter-stimulus interval, ISI) factorial design. The three types of pairs were (see **Fig. 4.3a**): *Identical*, where the same image was repeated, with the same physical properties and identity; *Within*, where the morphs came from the same side of identity boundary, but with 30% difference along the continuum; *Between*, where the morphs came from different side of identity boundary and also varied from the first member of the pair by 30% difference along the continuum. Note that the first face in each pair was always the same. Each pair was shown twice, once with a long (500ms) ISI between first and second faces, and once with a short ISI (75ms). Each face was presented for 500ms, with a 2500ms stimuli onset asynchrony (SOA) between pairs. The ISI manipulation was introduced to test whether iconic memory affects subjects' response patterns. The hypothesis was that stronger categorical perception will be observed in the long ISI and physical change effects will be mostly observed in the short ISI. Subjects were instructed to judge whether the two faces have the same or different identities. Subjects were advised that on occasion one identity might be presented with two different pictures. They were asked to respond as quickly and accurately as possible.

**Data analysis.** Data were analysed using Matlab6.0 and SPSS11.0. Results for 'different' responses were represented as a proportion of the total number of pairs per condition (i.e. out of  $43 \times 2$ ). All reported results are Greenhouse-Geisser corrected for violation of sphericity.

#### 4.4.2 Results & Discussion

Results are presented in **Figure 4.3b**. Participants judgements that stimulus pairs differed depended on their type ( $F_{1,4,13.9} = 80, P < 0.001$ ). As expected, pairs that straddled the categorical boundary (i.e *Between*) were more often judged as different than *Within* pairs ( $t_{10} = 7.9, P < 0.001$ ). There was also an additional (albeit smaller) effect of physical difference, with *Within* pairs more often judged as different than

*Identical* pairs ( $t_{10} = 4.5$ ,  $P < 0.005$ ). More 'different' responses were given to pairs that were presented with short ISI compared to long ISI ( $F_{1,12} = 18.6$ ;  $P < 0.001$ ). An interaction was also evident ( $F_{1.7,17.3} = 7.3$ ;  $P < 0.01$ ), with a tendency for the *Between* condition to elicit even more 'different' judgements at the short ISI compared to the long ISI ( $t_{10} = 4.7$ ,  $P < 0.05$ ) than the *Within* and *Identical* conditions. But note that similar overall behavioural patterns were observed at both ISIs (see Fig. 4.3b)



**Figure 4.3: Identity discrimination experiment**

**a.** Illustration of the three types of face-pairs used to produce the three main conditions (*Within*, *Identical* and *Between*) in the identity discrimination, fMRI and the priming experiments. Note that in all three conditions, the first face in a pair is equivalent, while only the second face varied to create the different pair-types. Note also that a given morphing level (e.g. 4<sup>th</sup> or 7<sup>th</sup> morph from the left along the x-axis in Fig. 4.1) could appear in either the *Identical* or the *Between* condition, depending on which of the counterbalanced stimulus-sets was used; see Methods. **b.** Results for the identity discrimination experiment: proportion of 'different' responses averaged across 13 subjects for the six different experimental conditions (see main text and Methods). Error bars represent SEM.

The results from this experiment confirmed that two faces straddling the putative ‘category boundary’ for identity were more likely to be judged as having different identities than two faces from the same side of the boundary, yet the faces in both pair types were equally separated along the morph continuum (**Figs. 4.1**). This finding accords with a previous report arguing for categorical perception of face identity (Beale and keil, 1995). Nonetheless, mere physical change along the morph continuum also influenced behavioural judgements, with *Within* conditions being judged ‘different’ slightly more often than *Identical* conditions. This suggests sensitivity to physical properties as well as to identity categories in the identity discrimination task.

The stronger effect observed here for categorical representation of identity might again be a mere task effect. As in the current experiment subjects were instructed to compare identities and not to base their judgement on physical cues between the images, hence biasing them towards categorizing identity while performing the same-different task. Therefore in the next experiment, I conducted an additional discrimination experiment, testing for categorical representations in a task based solely on physical aspects of an image.

## **4.5 PERCEPTUAL DISCRIMINATION TASK**

### **4.5.1 Methods**

**Subjects.** 13 volunteers (9 females, mean age 22, range 18-37y) participated. All had normal or corrected vision with no neurological or psychiatric history.

**Stimuli.** Subjects in this experiment saw four morphs from each continuum. The specific morphs were selected based on performance in the identity classification task (see above) that other subjects had undergone. Specifically, four morph levels generated two pair types of *Within* and *Between*, with the items of each pair being 30% apart along the continuum. It is important to note, that in this experiment the same morphs were used as in the previous experiment, but here we included both sets simultaneously (i.e. the Maggie and the Marilyn sets).

**Experimental procedure.** Prior to the experiment, subjects were exposed to the original morphs and provided a familiarity rating for them (see above). The experiment followed the *XAB* paradigm of (Bulthoff and Newell, 2004), where *X* is a cue face presented in the centre, followed by a *AB* face-pair presented simultaneously, side by side, in which *A* is the target (i.e. identical to the cue), while *B* is a distracter. The distracter can be either from the same side of the identity boundary (i.e. *Within*) or from the other side (i.e. *Between*). Note that in all cases the physical distance between the distracter and the target was 30%, thus any significant difference between the two distracter types could not be attributed to difference in physical similarity between the images (**Fig. 4.4a**). The cue/target morph could be any of the four morphs used, such that any order effects are counterbalanced. The subjects' task was to detect the location of the target face which was randomized. A total of 344 *XAB* trios per condition (43(pairs) x 2(*Within*, *Between*) x 2(end points) x 2 (direction of move on the continuum: to one end point or the other). A trial started with the presentation of an empty circle (500ms) to alert the subject, followed by the cue morph presented for 750ms. Then a fixation point for 250ms, and the face-pair presented for 750ms. A trial ended with a fixation point - total SOA 4s. The sequence was divided into five sessions, after each session the subject got feedback on his performances. Accuracy and reaction time were recorded.

**Data analysis.** Data were analysed using Matlab6.0 and SPSS11.0. Results for accuracy are represented as a proportion of the total number of trials per condition. Reaction times data were analysed only for corrected trials.

#### **4.5.2 Results & Discussion**

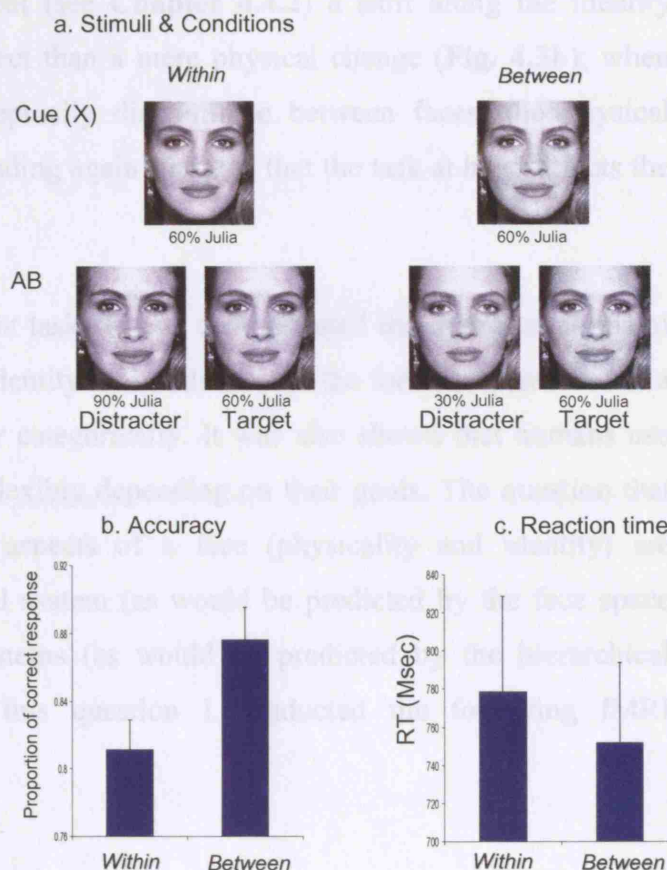
Results are presented in **Figure 4.4**. Subjects were better than chance (50%) at detecting the target in the *Within* condition ( $t_{12} = 18.2$ ,  $P < 0.001$ ) suggesting that they were sensitive to the 30% physical difference that was between the target and distracter. However they were even better at detecting the target when the distracter was straddling the categorical boundary (i.e. *Between*) than when it was from the same side of the boundary (i.e. *Within*,  $t_{12} = 10.5$ ,  $P < 0.001$ , **Fig. 4.4b**), even though the physical distance between the target and distracter in both conditions was the same (i.e. 30%). Moreover even in trials in which the target location was accurately



detected in the *Within* response time were longer compared to *Between* trios ( $t_{12} = 2.48$ ,  $P < 0.05$ , **Fig. 4.4c**) suggesting the former process was harder and more demanding.

**Figure 4.4: Perceptual discrimination experiment**

**a.** Illustration of the two types of Trios used to produce the two main conditions (*Within* and *Between*) in the experiment. **b.** Accuracy results presented as proportion and **c.** Reaction times results are for the correct responses averaged across 13 subjects for the two different experimental conditions (see main text and Methods). Error bars represented SEM.



The results from this experiment confirmed that two faces straddling the putative ‘category boundary’ for identity were less likely to be confused, compared to two faces from the same side of the boundary, even though the members of each pairs were equally separated along the morph continuum (**Fig. 4.4a**). These findings accord with the previous experiment reported here and a previous report arguing for categorical perception of face identity (Beale and Keil, 1995), but at the same time they provide also evidence for the physical representation of a face. The reaction time results suggest that physical discrimination between two morphs that are perceived to have the same identity is more costly than discriminating between two morphs that straddle the boundary. This supports the notion of an interaction between physical and identity representations, as identity influenced physical perception in these findings.

A comparison of the contribution of the physical difference (30%; *Within* – chance, 50%) and the identity boundary (*Between* – *Within*) in the perceptual discrimination task, revealed a larger effect for the physical differences than for the shift across the putative identity boundary ( $t_{12} = 13.9$ ,  $P < 0.001$ ). Interestingly, recall that in the identity discrimination experiment (see **Chapter 4.4.2**) a shift along the identity boundary had a much larger effect than a mere physical change (**Fig. 4.3b**); when subjects were required to perceptually discriminate between faces, the physical change effect was larger. This finding again suggests that the task at hand affects the way we perceive faces.

In conclusion, using four different tasks I have demonstrated that representations of faces contain both physical and identity information, with the former represented in a continuous fashion and the latter categorically. It was also shown that humans use these two types of information flexibly depending on their goals. The question that remains is whether these two aspects of a face (physicality and identity) are represented in the same neuronal system (as would be predicted by the face space models) or in two different systems (as would be predicted by the hierarchical models). In order to answer this question I conducted the following fMRI experiment.



# CHAPTER 5:

## DIFFERENT TYPES OF

## REPRESENTATION IN THE BRAIN –

## fMRI AND PRIMING EXPERIMENTS

---

### **5.1 PHYSICAL AND IDENTITY REPRESENTATIONS IN THE BRAIN – AN fMRI EXPERIMENT**

Only a handful of studies so far have used functional brain imaging combined with face morphing manipulations to investigate the neuronal representation of faces. Campanella et al. (2000) tested for a physiological marker indicative of categorical perception of unfamiliar faces using electrophysiological recordings. They showed an identity categorical effect in the N170 to pairs of faces, where the items in a pair were either from the side of a continuum or from opposite sides. These electrophysiological results are inconsistent with previous reports in the literature. Firstly, categorical perception was not observed for unfamiliar faces (Beale and Keil, 1995). Furthermore, repetition related decreases for identity are rarely reported to occur in the N170 but much later (George et al., 1997; Schweinberger et al., 2002; Henson et al., 2003).

Using PET Rossion et al., (2001) identified regions in the brain that tracked categorical perception of a familiarity signal. They generated morphed continua between familiar (newly-learned through repeated presentations) and unfamiliar faces. During scanning, subjects were presented with blocks of faces from six different locations along the continua. Results showed reduced activation to newly learned faces compared to novel faces in the right fusiform gyrus (FFG), right inferior occipital gyrus (IOG) and right middle occipital gyrus (MOG). Based on these findings, they claimed that the familiarity signal is categorical i.e. ‘all-or-none’, and that this categorical representation is not associated with activation of different regions in the brain, suggesting that familiar and unfamiliar faces activate the same neuronal network and differ only quantitatively (Rossion et al., 2001).

These studies provide some evidence for categorical representation of faces in the brain. They do not provide evidence for representation of the physical properties of a face, though as I demonstrated previously in the behavioural studies, the physical properties of a face are represented. Therefore the following fMRI experiment was designed to address this question: Are there representations of physical properties and identity of faces in the brain and are they anatomically dissociated as the hierarchical model predicts?

### ***5.1.1 Methods***

**Subjects.** 14 healthy right-handed volunteers participated (7 females, mean age 28, range 22-39y). All had normal vision and no concurrent or past neurological or psychiatric history. One subject failed to understand the monitoring task and was excluded from analysis.

**Stimuli.** In the imaging experiment we used stimuli and conditions analogous to the identity discrimination experiment see **Sec. 4.4.1** and **Figure 4.3a** (except that only 39 morph continua were now used, due to time constraints).

**Experimental procedure.** Prior to the experiment, subjects were exposed to the original morphs and gave their familiarity ratings for them as above. During fMRI, a pair-repetition paradigm was used (i.e the ‘adaptation’ paradigm; Grill-Spector et al., 1998; Kourtzi and Kanwisher, 2000). The factorial design was identical to the

identity discrimination experiment (see above) with a 3 (pair-types: *Within*, *Identical*, *Between*) by 2 (ISI: 75/500ms) design. Morphs were presented for 500ms with one or other ISI separating the two morphs, the SOA was 2500ms. The order of trials was pseudo randomised to maximize separation in time between repeating of morphs from the same continuum. Subjects were instructed to maintain fixation and to press a key only when a particular face-identity appeared, the target identity was randomly chosen from 3 continua that were excluded from the experimental design. These target events were used for the monitoring task and were modelled separately in the analyses. This task was chosen to avoid confounding the repetition manipulation with task demands. The experiment was divided into three phases (without a break in scanning) that started with presentation of a target identity (one of the three possibilities) and ended with feedback on performance. The experiment included 36 trials for each of the 6 conditions. A further ~25% of the total trials were null events in which only a fixation point was presented (Josephs and Henson, 2001), and ~15% of total trials were targets. The targets could appear as the first or the second face in a pair with either a long or a short ISI.

**Scanning.** A Siemens 3T Allegra system was used. 44 oblique axial slices (2 mm thick with 1mm gap) were acquired with 64\*64 pixels and in-plane resolution of 3\*3 mm<sup>2</sup>, 90° flip-angle, 30ms echo time (TE) and 2860s repeat time (TR). Subsequent to the functional scans, a T1 weighted structural image (1\*1\*1 mm resolution) was acquired for co-registration and display of the functional data. See **Chapter 2** for more details.

**Data analysis.** The whole-brain voxel-based analyses were performed with SPM2 ([www.fil.ion.ucl.ac.uk/spm](http://www.fil.ion.ucl.ac.uk/spm)). Pre-processing included spatial realignment, unwarping and temporal realignment (see **Chapter 2** for more details). To optimize the normalization, the segmented grey matter of the EPI image was normalized to a standard grey matter template corresponding to the MNI reference brain in Talairach space. The EPI images were then resampled with the parameters obtained from the above procedure to 3 x 3 x 3 mm<sup>3</sup>, smoothed with an isotropic 9 mm full-width-at-half-maximum (FWHM) Gaussian kernel.

In the first level analysis (**Chapter 2** and **Fig. 2.8**), single subject fMRI responses were modelled by a design matrix that consisted of the onset for the second event for each of the within-trial pairs for the 6 conditions, plus the target events, and the feedback at end of each phase. These 8 regressors were convolved with the canonical HRF. Note that with such short ISIs (75ms, 500ms), one cannot distinguish BOLD responses to the first and second face within each pair, meaning that the pairs are effectively treated as a single event (see also Winston et al., 2004); but recall also that the first face was kept constant for each continuum set, and conditions differed only in respect of the second face and its relationship to the first. To assess and control for pre-experimental familiarity with the faces (see below), I included as additional covariate regressors for each of the 6 conditions coded the mean familiarity rating of each subject with each face-pair (see **Figure 2.8**). Linear contrasts pertaining to the main effects, interactions and simple effects were calculated for each subject.

In the second level analysis, one sample t-tests were used with contrasts from the first level. The contrast images were first smoothed using a 3mm FWHM Gaussian kernel to account for residual inter-subject differences (final estimated smoothness was  $\sim 11 \times \sim 11 \times \sim 11 \text{ mm}^3$  FWHM). Simple effects were computed in SPSS using the parameter estimates (linearly transformed to percent signal change relative to the grand mean of the time course) extracted from the maxima that are presented in **Figures 5.1**. All reported results are Greenhouse-Geisser corrected to account for violation of sphericity.

### **5.1.2 Results & Discussion**

Sensitivity to **physical change** was tested by comparing the condition where the same physical stimulus was repeated against those conditions where there was a physical change (i.e. *Identical* < mean[*Within* + *Between*]) in a whole-brain analysis. Bilateral IOG showed less activation when physical properties were repeated compared to when they changed (**Table 5.1a**, **Fig. 5.1a**). A similar outcome was observed for the simple comparison of *Identical* < *Between* (right:  $t_{12} = 5.00$ ,  $P < 0.001$ ; left:  $t_{12} = 4.14$ ;  $P < 0.005$ ), which controlled for distance from the original unmorphed faces (hence from the ‘ends’ of the morph continua, see Methods).

Likewise, these regions also showed less activity in a simple comparison of *Identical* < *Within* conditions, where both conditions fall on the same side of the identity boundary while just physical aspects differ (right:  $t_{12} = 3.48$ ,  $P < 0.005$ ; left:  $t_{12} = 3.56$ ,  $P < 0.005$ ). There was no significant difference between the *Within* and *Between* pairs in these regions. This result suggests that bi-lateral IOG represents physical properties of a face independent of its identity.

Next, regions showing sensitivity to crossing the **identity** boundary were tested, initially by comparing conditions where the pair of faces remained on the same side of the identity border versus instances where they crossed it (*Between* > mean.[*Identical* + *Within*]). The right FFG showed less activation when identity was repeated compared to when it changed (Table 5.1b & Fig. 5.1b). A simple comparison of *Between* versus *Identical* also showed this effect ( $t_{12} = 4.28$ ,  $P < 0.005$ ), while controlling for distance from the original unmorphed faces (and hence from the ‘ends’ of the morph continua, see Methods). Similarly, the simple contrast of *Between* versus *Within* also showed this effect ( $t_{12} = 3.48$ ,  $P < 0.005$ ), while controlling for the presence of a 30% shift along the morph continuum. There was no significant difference between the *Identical* and *Within* conditions in that region. This result suggests that the right FFG represents facial identities independent of its physical properties.

Taken together, the above findings suggest a functional dissociation between posterior (occipital) and more anterior (fusiform) regions. To formally test for this dissociation, we performed an ANOVA now including region (left/right IOG, FFG) as well as conditions (*Within*, *Identical*, *Between*) as factors. This confirmed an interaction between regions (left IOG, right FFG) and conditions ( $F_{1,6} = 5.8$ ,  $P = 0.05$ ), due to the *Between* condition differing from the *Within* condition in the right FFG but not in the left IOG and the *Within* condition differing from the *Identical* in the left IOG but not in the right FFG. However, no such interaction was observed for the right IOG and the right FFG.

**Table 5.1**

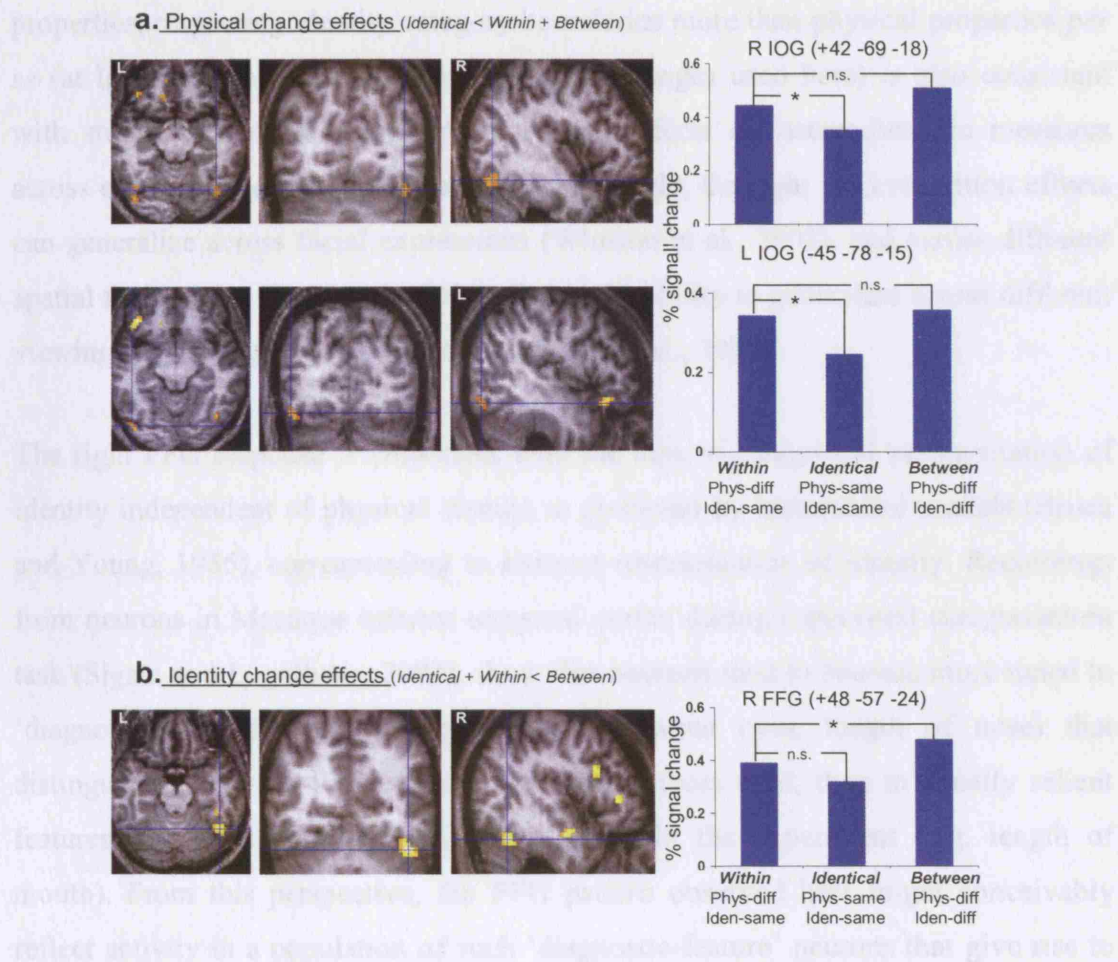
Anatomical Description			#voxels	Z score p<0.001	MNI x y z
<b>A. Physical Change effects</b>					
IOG	R	11	3.72		42 -69 -18
	L	12	3.68		-45 -78 -15
IFG	L	30	4.76		-39 30 -15
mOFCL		6	3.76		-9 42 -21
SFG	L	7	3.67		-9 45 48
<b>B. Identity Categorical effects</b>					
FFG	R	41	4.35		45 -57 -24
		6	3.26		33 -45 -27
LOS	R	8	3.39		33 -87 0
	L	5	3.35		-36 -90 -9
		8	3.28		-36 -78 -3
aSTS	R	16	4.25		48 -6 -21
IFG	R	10	3.97		48 36 3
	L	7	3.52		-33 36 -3
IFS	R	42	3.91		42 15 24

Abbreviations: IOG: inferior occipital gyrus; SFG: superior frontal gyrus; mOFC: middle orbital frontal cortex; FFG: fusiform gyrus; LOS: Lateral occipital sulcus; aSTS: anterior superior temporal sulcus; IFG: inferior frontal gyrus; IFS: inferior frontal sulcus; L: left; R: right hemisphere.

The fMRI results revealed different levels of face representation across distinct brain regions. The IOG was most sensitive to physical changes between face-pairs, regardless of whether these changes crossed an identity boundary. In contrast, right FFG was primarily sensitive to changes that crossed an identity boundary. This was found even when the presence of physical change was controlled, via comparison of a 30% shift within one side of the identity boundary against a 30% shift that crossed it.

These results accord with the hierarchical model of face processing where the initial stage encodes a view-specific representation of a face (Bruce and Young 1986), where variant aspects of a face are coded (Haxby et al., 2000), and is thought to be unaffected by face identity. Thus the sensitivity to subtle physical changes observed

in IOG activation makes this region a plausible candidate substrate for the initial structural encoding phase of faces.



**Figure 5.1 : fMRI results**

On the left, SPMs depicting **a.** the physical-change effects and **b.** identity-change effects (threshold  $P < 0.001$  uncorrected), overlaid on a T1 image of one subject. On the right, the histograms show average percent signal change for the three conditions (collapsed across ISI) taken from the maxima voxel marked with blue crosshairs, for which coordinates are given above each histogram. Zero in these histograms is the averaged signal along the entire scan.

In contrast, the right FFG showed sensitivity to identity change even when the presence of physical change along the morph continuum was controlled at 30%. This finding provides new evidence for some previous proposals that the FFG may play a role in differentiating between individual faces while generalizing across different viewing conditions (Haxby et al., 2000; Grill-Spector et al., 1999; Grill Spector et al., 2004). This finding can also be reconciled with single-cell evidence for units tuned to facial identity in regions that may be homologous to human FFG (Hassalmo et al.,

1989). It also fits with a recent report that epileptic activity in the right FFG can produce an inability to distinguish between faces (Mendez et al., 2003). The ability of an intact right FFG to generalize to some degree across different physical properties, respecting identity category boundaries more than physical properties *per se* (at least for the relatively subtle physical changes used here) is also consistent with studies that examined repetition-related effects on haemodynamic measures across other types of physical change. For example, the right FFG repetition effects can generalize across facial expressions (Winston et al., 2003), and across different spatial frequencies (Eger et al., 2004), though its ability to generalize across different viewing angles might be limited (Grill-Spector et al., 1999).

The right FFG response is consistent with the idea of categorical representation of identity independent of physical change as predicted by hierarchical models (Bruce and Young, 1986), corresponding to abstract representation of identity. Recordings from neurons in Macaque inferior temporal cortex during supervised categorization task (Sigala and Logothetis, 2002), show that neurons tend to become more tuned to ‘diagnostic’ visual features (e.g. distance between eyes, length of nose) that distinguished between the categories of cartoon faces used, than to equally salient features that were non-diagnostic of category in the experiment (e.g. length of mouth). From this perspective, the FFG pattern observed here might conceivably reflect activity in a population of such ‘diagnostic-feature’ neurons that give rise to categorical perception.

The results reported here are inconsistent with the predictions drawn from the face space models (Valantine, 1991; Tanaka et al., 1998), as the identity and the physical properties of a face were not represented in the same neuronal space but in two different anatomical structures. One possible way to accommodate the current results within the framework of face space models is by considering two spaces of representation: one of continuous representation of physical properties in the IOG, as early face space models have suggested (Valantine, 1991) and two an additional warped version of it in the FFG where attractor fields are created around identities (Tanaka et al., 1998).



The neuroimaging data reported here demonstrated that faces are represented in the occipito-temporal cortex in two ways: based on their physical characteristics and their identities. The next two experiments were designed to test the role of identity and physical representations in processing different types of information from a face. I used an immediate repetition priming paradigm and tested for modulation of response facilitation that is either influenced by physical properties of the face-pairs or by shared identity. The prediction was that for a given task, if response facilitation is observed for overlaps in perceived identity, then this task engages processes of identity mediated via the right FFG; however if no modulation of perceived identity is observed, then the task requirements do not rely on identity and hence are not modulated via the right FFG. A similar rationale was applied to infer modulation of physical properties from response facilitation. Two tasks were tested: a gender decision task that was hypothesized to engage processes related to physical aspects of face (see **Introduction** and **Chapter 4**) and a familiarity decision task that was hypothesized to engage identity related processes.

## **5.2 GENDER JUDGEMENT - PRIMING EXPERIMENT**

### **5.2.1 Methods**

**Subjects.** 12 volunteers (8 females, mean age 21, range 18-37y) participated. All had normal or corrected vision with no neurological or psychiatric history.

**Stimuli.** The set of stimuli used here were the same as in the identity discrimination and fMRI experiments, with three morph levels from each continuum. To avoid response bias, I equalized the number of females and males and used only 40 continua, by randomly excluding 3 male continua from the experimental stimuli set. These were used as fillers. In addition there were 48 (24 male) portrait photos of famous people who were edited to match the non-morphed original images and they served as additional fillers, to disguise the experimental structure.

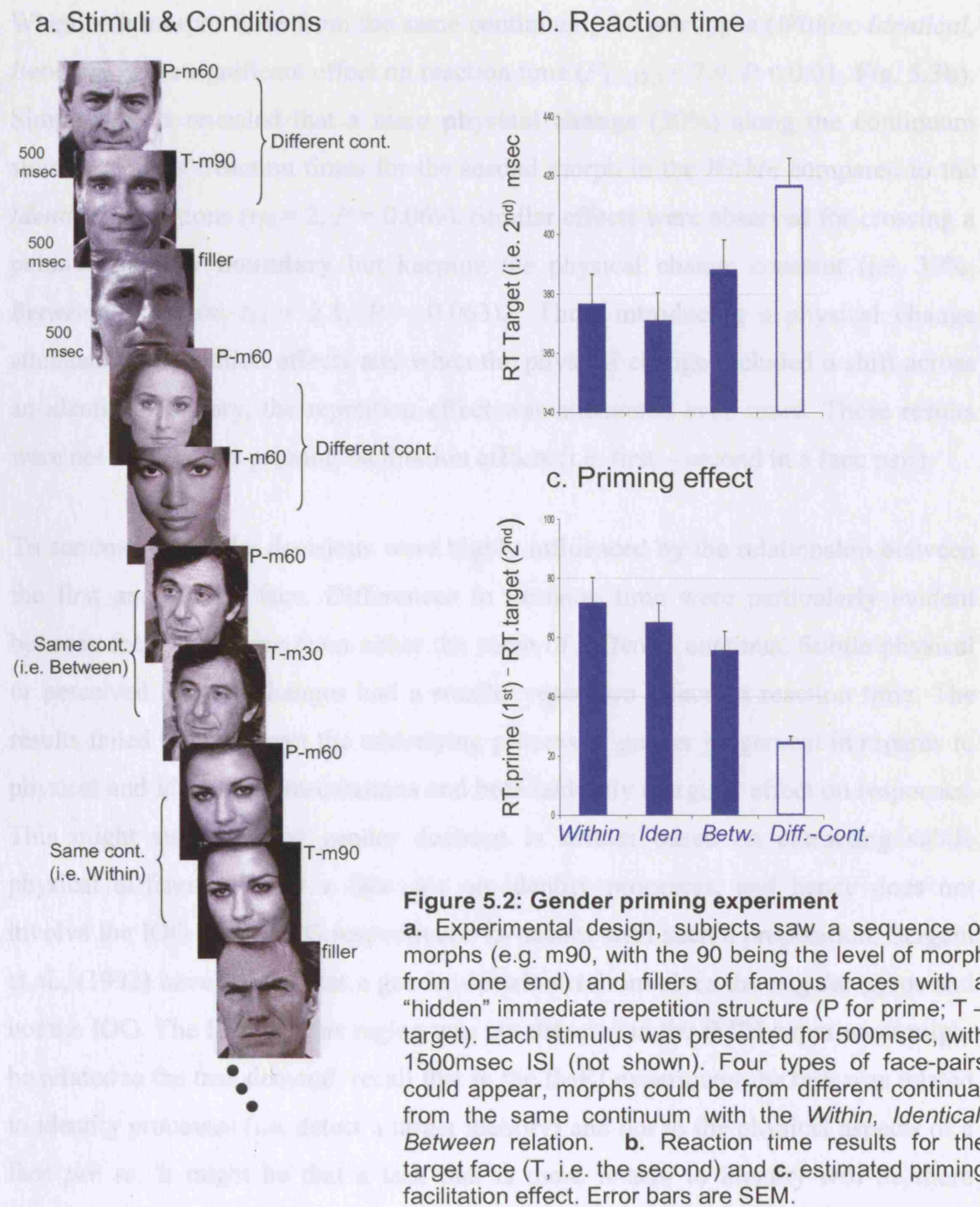
**Experimental procedure.** Prior to the experiment, subjects were exposed to the original morphs and to the fillers and gave their familiarity rating as above. The

experiment had 4 conditions: *Within*, *Identical* and *Between* and a condition where the two faces were not from the same continuum - *Diff.cont.* This last condition was added for two reasons: one to test for an effect of stronger physical changes that was produced by the different pictorial cues and second, it was used to control for variations in responses that is due to the location of the morph on the continuum. Thus, each of the three morph levels (**Fig. 5.2**) appeared in an additional face-pair where the first morph was from a different continuum. Note that across the whole experiment the same set of morphs were used but each time with a different pairing. Subjects were requested to indicate the gender of each stimulus using a button press. To control for priming due to facilitation of motor response, the gender of prime and target were always the same. Importantly, stimuli appeared in an on going sequence with no indication for the pair-repetition structure (**Fig. 5.2a**), fillers occurred 20% of the time. Each stimulus was presented for 500ms with an SOA of 1500ms. Reaction time for each stimulus was recorded. The sequences were divided into six sessions. Each started with five fillers and ended up by giving feedback to the subject of his/her performances.

**Data analysis.** Data were analysed using Matlab6.0 and SPSS11.0. Analysis was preformed only for pairs for which both primes and targets where correctly judged. The results are presented in the form of reaction time for the second morph, and as a measure of the priming facilitation effect. The priming facilitation effect was estimated by subtracting reaction time responses to the second morph from that of the first in each pair. Higher priming values indicate larger facilitation. All reported results are Greenhouse-Geisser correction for violation of sphericity.

### 5.2.2 Results & Discussion

Morph levels did not affect gender decision in the different continua conditions. This was tested in the conditions where the two morphs were not from the same continuum (RT:  $F_{1.9,17.9} = 0.48$ ,  $P = 0.6$ ). This suggests that the location *per se* of an image along the morph continuum did not affect performances on the gender decision task. Therefore, I collapsed responses across the different morphed levels of the second face for pairs where they were not from the same continuum.



Results are presented in **Figures 5.2b,c**. As can be seen when both faces were from the same continuum, subjects were quicker to judge the gender of the second morph ( $t_{10} = 7.87$ ,  $P < 0.001$ ) and showed stronger priming facilitation effect ([first – second]:  $t_{10} = 8.8$ ,  $P < 0.001$ ). These results indicate that gender decision involves processes that can be due to physical properties of a face, instantiated as pictorial cues in the image, or to identity change. As the two morphs in the *diff.cont* condition differ not only in the pictorial composition but also in their identity. Hence the next analysis aimed to tease these two processes apart.

When both morphs were from the same continuum, the pair types (*Within*, *Identical*, *Between*) had a significant effect on reaction time ( $F_{1.3,13.3} = 7.9$ ,  $P < 0.01$ , **Fig. 5.3b**). Simple effects revealed that a mere **physical change** (30%) along the continuum slowed subjects' reaction times for the second morph in the *Within* compared to the *Identical* conditions ( $t_{10} = 2$ ,  $P = 0.069$ ). Similar effects were observed for crossing a putative **identity boundary** but keeping the physical change constant (i.e. 30%, *Between* – *Within*;  $t_{10} = 2.1$ ,  $P = 0.063$ ). Thus, introducing a physical change attenuate the repetition effects and when the physical change included a shift across an identity boundary, the repetition effect was attenuated even more. These results were not observed as priming facilitation effects (i.e. first – second in a face pair).

To summarise, gender decisions were highly influenced by the relationship between the first and second face. Differences in decision time were particularly evident between faces that came from either the same or different continua. Subtle physical or perceived identity changes had a smaller repetition effect on reaction time. The results failed to tease apart the underlying process of gender judgement in regards to physical and identity representations and both had only marginal effect on responses. This might suggest that gender decision is neither based on extracting subtle physical differences from a face nor on identity processes, and hence does not involve the IOG or the FFG respectively. In accord with such a proposition, Sergent et al., (1992) have argued that a gender decision task involves the angular gyrus and not the IOG. The fact that this region was not detected in the fMRI experiment might be related to the task demand: recall that in the fMRI experiment the task was related to identity processes (i.e. detect a target identity) and not to the physical aspects of a face *per se*. It might be that a task that is more related to identity will be more sensitive at detecting difference between physical and identity processing. Therefore, I next tested priming effects in a familiarity judgement task.

## 5.3 FAMILIARITY JUDGEMENT PRIMING EXPERIMENT

### 5.3.1 Methods

**Subjects.** 12 volunteers (7 females, mean age 28, range 23-38y) participated. All had normal or corrected vision, with no neurological or psychiatric history.

**Stimuli.** The same set of stimuli were used here as in the prime-gender experiment. In addition, there were 116 portrait photos of unfamiliar faces for the task purposes. The unfamiliar portraits were chosen with care in order to minimize differences between these portraits and the ones of famous faces with regards to the composition of the photos: thus most unfamiliar faces were taken from models booklet or were unknown local politicians from around the world. Three independent judges rated these faces on familiarity to insure that the faces are indeed unfamiliar to Londoners. An additional 48 (24 male) portrait photos of famous faces served as fillers. All additional images were edited using Photoshop6.0 to match the size of the unmorphed original images.

**Experimental procedure.** Prior to the experiment, subjects were exposed to the original morphs and rated their familiarity with them, as above. The experiment had a similar design to the gender-prime experiment with 4 conditions: *Within*, *Identical*, *Between* and different continuum condition (*diff.cont* see above). The unfamiliar faces also appeared in pairs, where faces either repeated or changed. Subjects were requested to indicate for each stimulus whether it was familiar or unfamiliar by using a button press. Importantly, stimuli appeared in an on going sequence with no indication of the pair-repetition structure, with fillers occurring 20% of the time (**Fig. 5.2a**). Each stimulus was presented for 500ms with an SOA of 1500ms. The reaction time for each stimulus was recorded. The sequence was divided into six epochs: each started with five fillers and ended up by giving feedback to the subject of his/her performances.

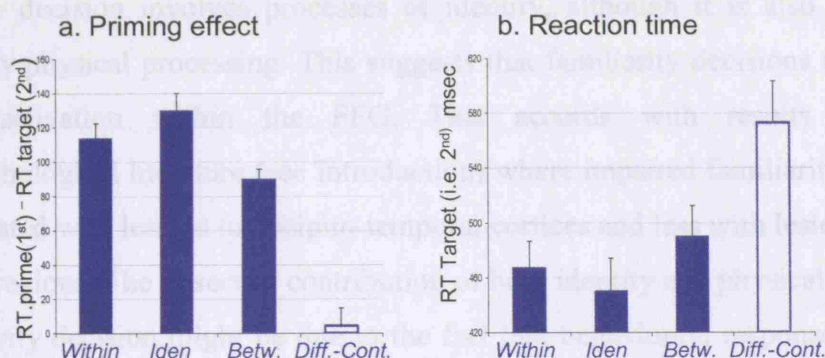
**Data analysis.** Similar analysis procedures were used as in the priming-gender experiment (see above). Only the famous face conditions were analysed and pairs included in the analysis were those in which correct responses were given for both first and second morphs.

### 5.3.2 Results & Discussion

Similar to the gender-priming experiment, there was no significant effect of morph levels on familiarity decision. This was tested in the conditions where the two morphs were not from the same continuum (RT:  $F_{1,9,21.9} = 2.83$ ,  $P = 0.08$ ). This



suggests that the location of an image along the morph continuum did not affect performances on familiarity decision tasks. Therefore, I collapsed responses for this condition, across the different morphed levels of the second face.



**Figure 5.3: Familiarity priming experiment**

**a.** Reaction time for the target, i.e. second face for the four experimental conditions: Same continuum: Within, Identical (Iden), Between (Betw.) and the different continua (Diff.-Cont.) pairs. **b.** Results for the priming facilitation estimation

Similar to the gender judgement experiment, responses for the second morphs were much faster if the first was from the same continuum than from a different one ( $t_{11} = 7.85$ ,  $P < 0.001$ ; **Fig. 5.3a**). This effect was also observed as a priming facilitation effect ( $t_{11} = 8.95$ ,  $P < 0.001$ ; **Fig. 5.3b**). These results indicate that a familiarity decision, similar to gender judgement, relies strongly on pictorial cues encompassing both physical properties of a face and its identity. Hence, the next analysis aimed to tease these two processes apart.

When both morphs were from the same continuum, the pair types (*Within*, *Identical*, *Between*) had a significant effect on reaction time ( $F_{1,9,21.6} = 12.5$ ,  $P < 0.001$ ) and on priming facilitation ( $F_{1,7,19.3} = 11.9$ ,  $P < 0.001$ ). Simple effects revealed that a mere **physical change** (*Within* – *Identical*) had a marginal effect on familiarity judgement, leading to slower reaction times, and weaker response facilitation for pairs that differed physically (i.e. 30%) compared to those that did not (*Within* – *Identical*; RT:  $t_{11} = 2.1$ ,  $P = 0.057$ ; priming:  $t_{11} = 1.9$ ,  $P = 0.086$ ).

In contrast to the small effect of physical change, there was a clear and robust effect of **identity change** on reaction time and response facilitation. Hence, crossing a putative identity boundary even when physical change was kept constant (*Between* –

*Within*), slowed reaction times and attenuated the facilitation of responses by priming (RT:  $t_{11} = 2.7$ ,  $P < 0.05$ ; priming:  $t_{11} = 2.5$ ,  $P < 0.05$ ).

As predicted, the results from the familiarity priming experiment suggest that familiarity decision involves processes of identity, although it is also marginally affected by physical processing. This suggests that familiarity decisions rely mostly on the activation within the FFG. This accords with results from the neuropsychological literature (see Introduction) where impaired familiarity decisions are associated with lesions to occipito-temporal cortices and less with lesions to more posterior regions. The observed contribution of both identity and physical processing to familiarity decision might be due to the fact that behavioural responses are most likely reflect outcomes of different neuronal systems and processes that operate in parallel or sequentially. Hence, it is not surprising that both types of representations were evident to some extent in the priming experiments results and in all the behavioural results presented before.

## 5.4 EFFECTS OF PRE-EXPERIMENTAL FAMILIARITY

Categorical perception is argued to be acquired (Harnad 1988), hence a knowledge regarding the characteristics of a category are essential before such a boundary can be established and categorical perception can arise. In relation to faces it has been demonstrated that when a face-pair is unfamiliar, categorical perception of an identity does not occur (Beale and Keil, 1995, though see Campanella et al., 2000, and Rossion et al., 2001). The aim of this analysis is to test whether the extent of familiarity with the famous faces modulates the identity categorical effects observed in perception and in the brain.

In order to test the effect of prior experience, **prior to all experiments** subjects gave familiarity ratings for each of the original (unmorphed) faces. For each face they were asked to indicate how well they knew that person, following a scale from 0-to-3 (0 – “don’t recognize at all”; 1 – “the face looks familiar”; 2 – “I have contextual information regarding that person” (e.g. she is a movie star); and 3 – “I know this

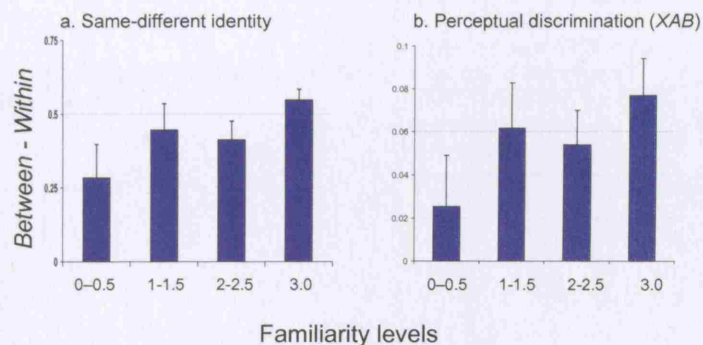
person well and can name him/her”). For each continuum I obtained a pre-experimental familiarity score by averaging the rating of its end-point faces. Note, that the experiments were not designed to test for these familiarity effects, hence the design and stimuli were not optimized (i.e. no unfamiliar faces were included) and only few faces were rated as complete unknown by subjects. Given the extended number of morphed continuum used (i.e. 43) some variability in pre-experimental familiarity was evident in subjects rating, allowing preliminary tests of such effects.

#### 5.4.1 Perceptual modulation by pre-experimental familiarity

Familiarity did not significantly modulate responses in the identity classification task, nor in the similarity judgement task. However, a significant effect was observed in the identity discrimination experiment at the inter- and intra-subject levels. Mean pre-experimental familiarity per subject correlated positively ( $r = 0.798$ ,  $P < 0.005$ ) with the effect of *Between - Within* conditions on rate of ‘different’ judgements. A similar effect was observed when testing it at the intra-subjects levels, i.e. assigning each morph-pair to a different familiarity level depending on individual subject ratings. A significant linear increase ( $F_{1,11} = 6.87$ ,  $P < 0.05$ ) with larger categorical effects for morphs that were more familiar to the subjects (**Fig. 5.5a**). In other words, when faces were more familiar to the subjects, the difference of *Between - Within* was larger; thus pairs were more likely to be judged as having ‘different’ identity when they straddled an identity boundary, while controlling for the presence of a shift along this continuum by comparison with the *Within* case.

**Figure 5.4: Effect of familiarity on perception**

Effects of subjects’ familiarity with the faces on the categorical perception estimated as *Between - Within* **a.** in the identity discrimination experiment. **b.** in the perceptual discrimination experiment



A similar effect was observed in the perceptual discrimination task (**Fig. 5.4b**), but it was not significant either at the inter subjects level ( $r = 0.4$ ,  $P = 0.1$ ) or as a linear component at the intra-subject level ( $F_{1,11} = 2.1$ ,  $P = 0.17$ ). When comparing continua where both faces



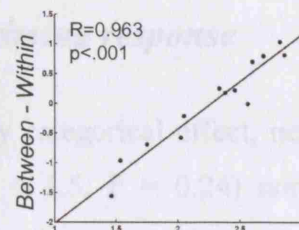
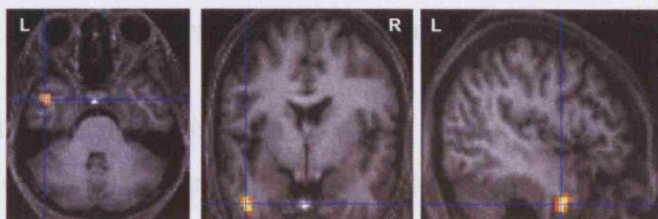
are unknown compared to all other continua, a significant difference was observed ( $t_{10} = 1.8$ ,  $P < 0.05$ , one tailed), with unknown pairs showing a weaker identity categorical effect compared to known pairs. This result confirms previous reported observations (Beale and Keil, 1995) that categorical perception depends on prior familiarity with faces.

The extent of familiarity with a face did not modulate the sensitivity to physical change in a face in either the identity or the perceptual discrimination tasks.

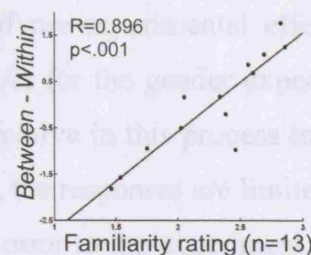
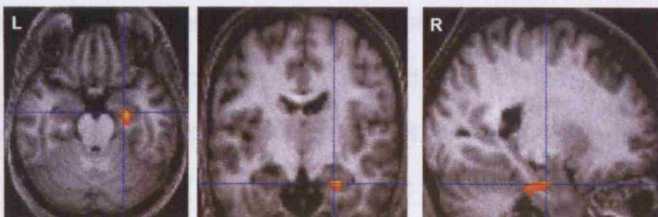
#### ***5.4.2 Extent of familiarity modulates brain sensitivity to changes in faces***

Pre-experimental familiarity modulations of brain sensitivity to identity change were observed at the inter-subject level. Here, sensitivity to identity change was assessed by the *Between* – *Within* comparison that controls for the presence of physical change. Recall, that it was this comparison that had shown a correlation with inter-subject pre-experimental familiarity in the behavioural study. The difference in activity for *Between* minus *Within* conditions correlated positively with inter-subject differences in the extent of pre-experimental familiarity (being more pronounced in those who were more familiar with the faces) in the bilateral anterior temporal pole (aTP), and in the right anterior hippocampus (**Fig. 5.6, Table 5.2**). Note that these regions showed no reliable main effect of identity change when subjects' familiarity was not considered. This profile contrasts with the right FFG region, which showed an effect of identity change (see above), but no evidence of modulation by the extent of pre-experimental familiarity (FFG:  $r=0.25$ ,  $Z=0.23$ ,  $p=0.41$ ).

## L anterior temporal pole (-45 0 -39)



## R Hippocampus (+24 -12 -27)



**Figure 5.5: Effect of pre experimental familiarity – fMRI**

On the left, statistical parametric maps for regions showing a positive correlation between inter-subject pre-experimental familiarity and the BOLD effect of identity-change, when the presence of a physical shift along the morph continua was controlled (i.e. for *Between* > *Within*), thresholded at  $p < .001$  (uncorrected) and overlaid on a T1 image of one subject. The graphs on the right show scatter-plots for subjects' mean pre-experimental familiarity ratings on the whole face set (x-axis), against their identity-change fMRI effect (y-axis) with a fitted regression line, for the left anterior temporal pole and right anterior hippocampus.

**Table 5.2: effects related to pre-experimental familiarity**

Anatomical Description	#voxels	Z score ( $p < 0.001$ )	MNI x y z
<b>A. Inter-subject - Positive correlation familiarity &amp; identity: Familiarity &amp; (<i>Between</i> - <i>Within</i>)</b>			
aTP L	26	5.27	-45 0 -39
R	1	3.09	63 -6 -33
aHipp R	34	4.14	24 -12 -27
SFG L	28	4.16	-6 18 69
<b>B. Inter-subject - Positive correlation familiarity &amp; physical: Familiarity &amp; (<i>Within</i> - <i>Identical</i>)</b>			
Calcarine sulcus	46	4.47	18 -87 15
CG	8	3.77	12 18 48

Abbreviations: aTP: anterior temporal pole; mOFC: medial orbital frontal cortex; LF: lateral fissure; STG: superior temporal gyrus; aHipp: anterior hippocampus; SFG: superior frontal gyrus; aSTS: anterior superior temporal sulcus CG: cingulate gyrus; L: left; R: right hemisphere.

### ***5.4.3 Familiarity modulation of facilitation priming response***

The extent of familiarity did not modulate an identity categorical effect, neither in the gender judgement task (Linear component:  $F_{1,9} = 1.5$ ,  $P = 0.24$ ) nor in the familiarity decision tasks ( $F_{1,10} = 0.35$ ,  $P = 0.85$ ). The last comparison was tested only on pairs with familiarity levels of 1.5 and above, as there were not enough correct responses for less familiar pairs. The lack of pre-experimental effects on identity categorical priming effects is not surprising. As for the gender experiment, there was weak evidence that identity processes are involved in this process to begin with (see 5.2). With regards to the familiarity decision, the responses are limited only to those faces with which subjects were familiar with prior to the experiment, hence rendering the design insensitive to any possible effect of pre-experimental familiarity.

## **5.5 GENERAL DISCUSSION**

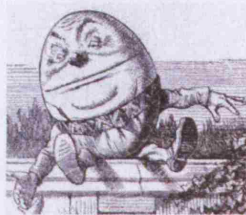
The aim of this part of the thesis was to explore the hierarchical structure of face identity processing. As predicted, evidence for physical and identity representations of faces was observed. It was also shown that the goal of the observer (i.e. task requirement) affects which of these two types of representation is most likely to be used, with similarity judgements and perceptual discrimination relying more on continuous physical representations and identity classification and discrimination relying more on categorical identity representations. Second, I demonstrated that these two processes are dissociated anatomically in the brain, and this hierarchy is along a posterior-anterior anatomical axis. Posterior regions (IOG) represent physical properties of a face while more anterior regions (FFG) represent the identity of a face. An additional level of the hierarchical structure of identity involved anterior temporal regions (aTP, aHipp). These regions modulated their sensitivity to identity change as a function of the extent of subjects' familiarity with the face set and are suggested to be involved in representing semantic information. An additional priming experiment revealed that familiarity decisions are affected by shifts across

identity boundaries. Hence it is suggested that familiarity decision involves processes within the FFG. The absence of modulation by the extent of familiarity with the faces in the familiarity priming experiment might suggest that these processes did not involve representations encoded in the anterior temporal pole. In contrast, the priming gender experiment did not show robust effects of either identity or physical changes in the morphs. This might suggest that gender decision primarily involves other regions than the ones observed in this fMRI experiment.

Building on these results, the aim of the next chapter is to explore in more detail the type of representations and processes that occur in the early stages of face processes, specifically focusing on posterior occipital regions.

## PART III:

# EARLY FACE PROCESSES



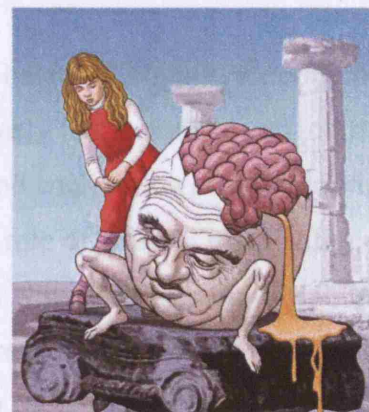
*"I should know you again if we did meet,"  
Humpty Dumpty replied in a discontented tone...  
"You're so exactly like the other people."*

*"The face is what one goes by, generally," Alice remarked in a thoughtful tone.*

*"That's just what I complain of," Said Humpty Dumpty.*

*"Your face is the same as everybody has - the two eyes, so-"(marking their places in the air with his thumbs) "nose in the middle, mouth under. It is always the same. Now if you had the two eyes on the same side of the nose, for instance - or the mouth at the top - that would be some help."*

(Lewis Carroll, Alice in Wonderland).



In their seminal paper ‘understanding face recognition’ Bruce and Young (1986) acknowledged that the description of early face processes i.e. the *structural encoding phase* was vague and underspecified, and that more work was needed to establish a more precise specification of this phase. The aim of this part of the thesis is to explore the question as to what precisely early face processing encompasses.

This part of the thesis was based on two working assumptions. The first, a functional assumption, postulated that distinct types of visual face information are processed separately in early stages, while at later stages this information is integrated to generate the conscious perception of a face as we experience it. The second assumption relates to the neurophysiological structure of the brain: where it is assumed that posterior occipital regions are associated with lower levels of computation than those occurring in more anterior regions, in effect reflecting a posterior – anterior hierarchical gradient as observed in Chapter 6.

Two types of functional dissociations were investigated. The first (**Chapter 6**) relates to the nature of the visual input to the cortex. Specifically, there are two different pathways by which visual information projects to the cortex: the parvo- and the magno cellular pathways. These two pathways differ in the spatial frequency information they convey. The experiment tests for anatomical dissociation in posterior occipital cortices between processes related to the different spatial frequency bands (SF). The chapter includes a review of the relevant literature on spatial frequency role in face processing and the presentation of an fMRI experiment.

The second functional dissociation that was tested is based on cognitive definitions of the different types of information within a face, namely features and configuration (**Chapter 7**). Again, it starts with a literature review and continues with a description of a behavioural and an imaging work that tested the role of featural and configural information in face processing. The chapter concludes with a description of a follow up behavioural work that focused on individual differences in sensitivity to featural and configural information and the way in which this sensitivity affects face recognition.

# CHAPTER 6:

## PROCESSING SPATIAL

## INFORMATION FROM A FACE

---

### 6.1 INTRODUCTION

#### *6.1.1 Two sub-cortical visual pathways*

In a visual scene, luminance and contrast changes can be described along a frequency dimension. Using Fourier's algorithms it is possible to transform the spatial information in an image into spectra of frequencies (Campbell and Green, 1965). Slow changes of luminance in an image can then be described as low spatial frequency (LSF) information. An image that contains only LSF information looks fuzzy and blurred depicting mostly crude information in the image (see **Fig. 6.1**). On the other hand, rapid and abrupt changes of luminance (such as contour lines) can be described as having mostly high spatial frequency (HSF) information. A line drawing is an example of an image that contains mostly HSF information (see **Fig. 6.1**). HSF information is associated with the fine detailed information in an image (Morrison and Schyns, 2001).

Somewhat surprisingly (as for us humans we cannot consciously dissociate the information from different frequencies) it turns out that processes that take place in the mammals' eye can be described using spatial frequency filters, where the visual input is separated into different SF components (see de Valois and de Valois, 1990 for review). The different frequencies are conveyed by two sub-cortical pathways: the magno- and the parvo-cellular (MC, PC, respectively). These two pathways



express different types of information regarding a stimulus (Hubel and Wiesel, 1977; Bullier, 2001; Bar, 2003; Lamme, 2001). MC inputs have larger receptive fields and are more sensitive to LSF information ( $SF < 1.5$  cycle/degree, Skottun, 2000). MC inputs are also sensitive to rapid temporal changes in the environment especially in the periphery and convey information faster than the PC pathway (Nowak and Bullier, 1997). The latter by comparison has smaller receptive fields and is more sensitive to HSF information ( $SF > 1.5$  cycle/degree, Skottun, 2000), colours and foveal vision. Thus these two pathways can be described as providing a coarse and fine representation of the visual world, respectively (Bullier, 2001; Bar, 2003). Based on neurophysiology research, it has been suggested that to some extent the SF segregation is maintained beyond V1/V2 (i.e. in higher visual areas; Shipp and Zeki, 1995). Furthermore, it is known that the dorsal pathway, especially the middle temporal cortices, receives the majority of its input from the MC pathway (Shipp, 2001). Psychophysical research using adaptation techniques have also demonstrated that these SF channels could be selectively compromised, suggesting a degree of independence (e.g. Blackmore and Campbell, 1969).

### ***6.1.2 The coarse-to-fine and the flexible usage hypotheses***

The *coarse-to-fine* hypothesis is one of the most influential ideas regarding the differential role of low SF (i.e. coarse) and high SF (i.e. fine) in processing visual information (e.g. Mar, 1982; Parker and Costen, 1999, Lamme 2001; Bullier, 2001; Bar 2003). This hypothesis states that low SF information arrives in the brain before high SF (see above) and generates an initial coarse image representation that constrains and facilitates the latter high SF processing that extracts fine detailed information from an image.

Using complex visual stimuli and faces, Parker et al. (1992) were the first to provide evidence for the *coarse-to-fine* hypothesis. They presented subjects with a rapid sequence of spatially filtered images, in two different orders either LSF-then-HSF or HSF-then-LSF. They showed that subjects perceived the first sequence, LSF-then-HSF as having a better quality compare to the second (Parker et al., 1992). In a different experiment, subjects mistook more frequently the LSF-then-HSF sequence as being a non-filtered image compare to the HSF-then-LSF sequences (Parker et al.,



1997). A similar advantage in processing LSF-then-HSF sequences was demonstrated using hybrid images (Schyns and Oliva, 1994).

Based on neurophysiological findings, several neuroanatomical models have been proposed for this *coarse-to-fine* hypothesis (Lamme, 2001; Bullier, 2001; Bar, 2003). MC pathways are suggested to generate an initial crude representation in V2 (Lamme, 2001), in dorsal parieto-occipital regions (Bullier, 2001) or in frontal cortices (Bar, 2003). The crude representation is then projected back to early visual areas (Lamme, 2001; Bullier, 2001) or to the ventral stream (Bar, 2003) to facilitate fine detailed analysis and to guide the binding of features into a whole object.

A *flexible usage* of the SF hypothesis was suggested by Morrison and Schyns (2001). Here, LSF and HSF information are used flexibly, depending on the goal of the observer. Using hybrid SF faces (e.g. LSF extracted from an angry female face and superimposed on an HSF image of a happy male face) they demonstrate that different tasks recruit different SF information (Schyns and Oliva, 1999). For example, judgement of whether a face is expressive or not is more dependent on the HSF information, while categorization of the expression relies more on LSF information than HSF. These findings suggest that distinct task demands influence the type of information extracted from different SF channels, which means that they remain dissociable to some extent and that they are susceptible to top down modulation.

### ***6.1.3 SF information and facial identity processing***

SF information has also been investigated in the context of identity processing with the aim to determine the critical bandwidth for face identity processing. Some researchers have shown that LSF information is particularly important for encoding face identity (Harmon, 1973; Ginsburg, 1978), though others challenge the LSF information superiority hypothesis and suggest that HSF information is more important for face recognition (Fiorentini et al., 1983, Vuilleumier et al., 2003) or that the critical bandwidth for identification is in the middle SF range (8-13 cycle/face, Nasanen, 1999; Ojanapaa and Nasanen, 2003).

An interesting study by Le Grand et al. (2003) has reported that early deprivation of LSF visual information (due to cataract at birth) impairs configural processing of a

face. This suggests some role of LSF in face processing, though the effect on face processing beyond the lab context was not reported (Le Grand et al., 2003) for example do these patients have impaired face perception, or impaired face recognition?

The differential role of SF information in face processing has also been investigated using electrophysiological methods. Recordings from face selective cells in macaques' superior temporal sulcus did not report any differential SF responses, i.e. the cells responded equally well to a filtered face with either HSF or LSF information (Rolls et al., 1985). Intracranial ERP studies have demonstrated that N200 (a face specific ERP wave) recorded from humans' ventral occipito-temporal cortex is weaker and emerges later for line drawing (i.e. HSF) compared to blurred (i.e. LSF) faces. Similar results were obtained using scalp recording, in which weaker N170 responses were observed for HSF compared to LSF and full band faces (Goffaux et al., 2003a), an effect that was also modulated by task (Goffaux et al., 2003b).

#### ***6.1.4 Computational models***

Daily and Cottrell (1999) created a neuronal network with two modules, each receiving a different SF input. They trained the network on two tasks: the first task was to distinguish between faces and different types of objects (e.g. cups, books) and presumably reflects face detection mechanism; the second task was to distinguish between individual faces, and hence taps to recognition processes. They found that the module that received low SF input was more efficient in categorizing faces from different objects and was also more dominant in a face identity discrimination task. They concluded that a specialized face processor -for detecting and recognizing faces- is likely to rely more on low than high SF information (Daily and Cottrell, 1999).

The lattice model (Lades et al., 1993) is another computational network that separates an image into different SF bands. This network has two layers. The first layer is a matrix superimposed on a 2-D image (such as the image encoded by the eye), with each point of the matrix acting as the centre of a receptive field. An image

is described in terms of the different SF components and their 2D orientations at each point. This is achieved by using a set of kernel functions called *Gabor jets*. The second layer of the network is suggested to store information about a particular face using a similar matrix layout. Having limited warping between the two representations allows for a match or non-match decision to be obtained for recognition purposes.

In order to increase efficiency and reduce the degrees of freedom in this matrix, Wiskott et al., (1997) suggested fixing points (jets) based on a-priori knowledge of the canonical structure of a face (1<sup>st</sup> order configuration), i.e. critical landmarks, such as the corner of the eyes, eyebrow etc. These points are termed *fiducial points*. The location of the *fiducial points* is encoded with respect to a prototypical face (Biederman and Kalocsai, 1997). Using this method it was possible to demonstrate how face recognition can be achieved by decomposing a face into different SF information components and comparing the output to a stored representation with a similar format (i.e. second layer). Such a model would predict separate representations of different SF bandwidths and that regions that are involved in face recognition (as suggested here the FFG, see **Chapters 1, 5**) maintain the SF separation (i.e. different *Gabor jets*). This computational network also suggests also that all SF bands are critical to face processing.

### **6.1.5 Neuroimaging studies**

Despite a considerable literature on the role of SF in face processing, there have been remarkably few neuroimaging studies to date using face-stimuli at different bandwidths. Two recent fMRI studies reported differential activations for high- and low-pass faces during a gender-decision task (Vuilleumier et al., 2003; Eger et al., 2004). Specifically, bilateral FFG and IOG showed stronger activation for HSF faces than LSF faces (Vuilleumier et al., 2003; Eger et al., 2004). Conversely, LSF faces show stronger activation in bilateral parieto-occipital cortex (Vuilleumier et al. 2003), or in the calcarine sulcus (Eger et al., 2004). Others (Iidaka et al., 2004) argue for hemispheric differences and showed that only the left FFG and the left IOG responding more strongly to HSF compared to LSF filtered faces and houses - neither hemisphere showed larger activation for LSF compared to HSF visual

information (Iidaka et al., 2004). Integration of LSF and HSF information from a face was observed in the FFG (Vulleumier et al., 2003; Eger et al., 2004).

One caveat of the above studies is that the SF manipulation is confounded with other visual differences between the filtered images (e.g. contrast, energy, luminance). More importantly, stimulating only partial SF bands might have led to changes in face processing strategy in order to adapt to the limited amount of information available (see also Morrison and Schyns, 1999). Therefore, in the present fMRI study, I avoided any effects due to stimulation of only one or other SF range, by always presenting information in both HSF and LSF ranges conjointly, using 'hybrid' stimuli. In a hybrid image different LSF and HSF filtered faces are superimposed (e.g. Schyns and Oliva, 1999; see **Fig. 6.1**). This technique has previously been used successfully in one other fMRI study (Winston et al., 2003). However, this latter study focused on the role of distinct SF for processing facial expression, whereas the present study is specifically concerned with neural activity associated with repetition of face identity in different SF ranges, i.e. testing the SF effects of face individuation processing.

Here, differential SF sensitivity was tested using an immediate repetition paradigm (i.e. fMRI-adaptation paradigm Grill-Spector et al., 1999). Within the hybrid stimulus, a given HSF or LSF face could be either repeated or changed across successive trials independently (**Fig. 6.1**). The rationale behind the analyses was that sensitivity to a particular SF (say, LSF information), would be revealed by repetition-related decreases in activation specific to that particular SF range (e.g. decreases for repetition of LSF information). By contrast, the same region would not be affected by repetition in the other range (e.g. HSF). Any brain region mediating face processing that can draw on face information from both SF ranges should be modulated by repetitions in either LSF or HSF.

Finally, I manipulated the observer's attention to one or other SF range during presentation of the hybrid faces. This was done in order to avoid uncontrolled spontaneous allocation of attention to one particular range. It also enabled me to test whether repetition for a given SF range might depend on selective attention to that range. Moreover, directing attention to specific aspects of sensory stimuli is known

to enhance fMRI evoked responses in brain regions that are involved in processing those attended aspects (O'Craven et al., 1999; Vuilleumier et al., 2001). Note that in this instance, the predicted effects of attention is in the opposite direction to the predicted effect of stimulus repetition, evoking an increased activation for attended properties (O'Craven et al., 1999) rather than decreased activation for repeated properties of a particular stimulus (Grill-Spector et al., 1999, 2001; Eger et al., 2004; Rotshtein et al., 2005).

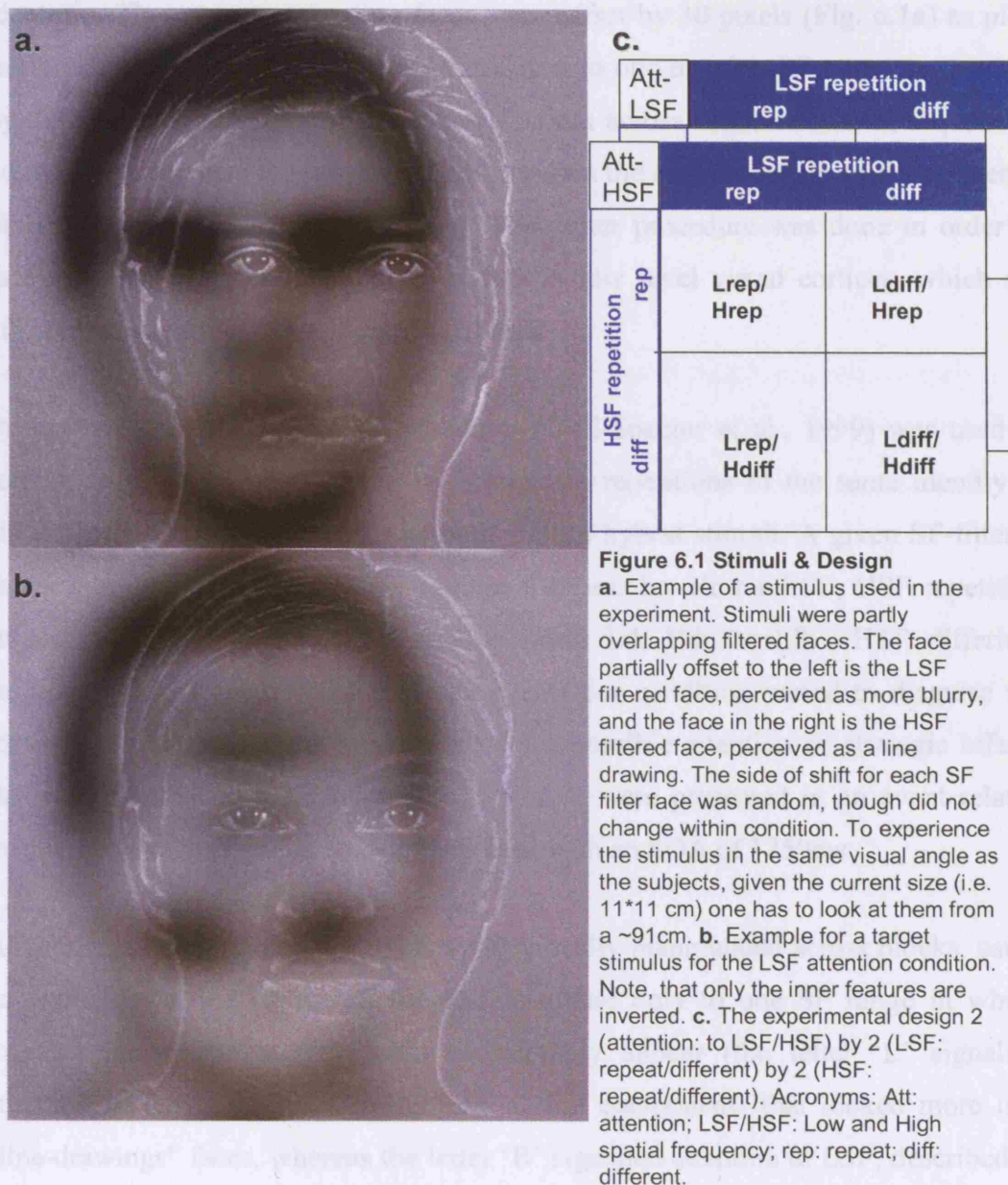
## 6.2 METHODS

**Subjects.** 15 healthy volunteers participated in the brain imaging experiment (8 females, mean age 29.5y, range 22-43y, all right handed). All had normal vision, no past neurological or psychiatric history and no structural brain abnormality. One subject failed to perform the task and was excluded from the analysis.

**Stimuli.** 56 faces (28 females) with neutral expression were chosen from the Karolinska Directed Emotional Faces set (KDEF, Lundqvist and Litton, 1998). 56 faces with fearful expression<sup>1</sup> and 18 additional faces from the same set served as fillers (see below). Faces (experimental and fillers) were achromatic and edited so that different 'inner' facial features were placed within an identical unisex face outline (i.e. hair style, ears, chin contour, neck and shoulders, see **Fig. 6.1a**). This latter manipulation was implemented to avoid a possible confound due to different SF information in the 'outer' and 'inner' features of a face, as it is likely that 'outer' features varied more in LSF than in HSF range. Moreover, I wanted to constrain the effect of the experimental manipulation to the 'inner' features of a face, as it is commonly assumed that they are more crucial for face processing than 'outer' features (Haig, 1986). In addition, oddball target stimuli (**Fig. 6.1b**), were created by inverting the inner face features within the upright outline. The final image resolution was 512\*512 pixels with view angle of 6.8°.

---

<sup>1</sup> This experiment originally had another factor - the expression of a face (i.e. neutral or fearful). Due to an error in the programming of the experiment one cell was not presented to the subjects, creating an incomplete factorial design with a missing cell. As it turned out, the expression of a face had a big effect on the results, but due to the missing cell these results were uninterruptible. Therefore, in all the subsequent analysis I did not include the faces with the fearful expressions and they were treated as fillers. This obviously resulted in lost of sensitivity, as more than half of the stimuli in the experiment were not included in the final analysis.



Using Fourier transformation, the images were transformed to frequency space and were filtered using a Butterworth filter (Winston et al., 2003), set to high pass ( $SF > 24$  cycle/image; viewed as  $SF > 3.52$  cycle/degree) or low pass ( $SF < 8$  cycle/image; viewed as  $SF < 1.17$  cycle/degree). The distance between these filtered faces was 1.5 octaves to minimize overlaps. This cut-off was chosen to fit previous findings suggesting that MC visual pathways are sensitive to SF below 1.5cycle/degree while PC pathways are sensitive to SF above it (Skottun, 2000). After filtering, each SF band was transformed back to the spatial dimension. Each 'hybrid' stimulus was composed of two partly overlapping filtered faces (i.e. HSF and LSF) with different

identities. These two overlapping faces were offset by 30 pixels (**Fig. 6.1a**) as pilot testing showed it facilitated selective attention to one or other SF range as required by the task. The direction of offset was random across different stimuli sequences, but was kept constant for subsequent trials within the same sequence (e.g. a sequence of HSF repetition and LSF changing). This latter procedure was done in order to facilitate adaptation of neuronal responses in low level visual cortices, which are affected by stimuli location in the visual field.

**Procedure.** An fMR-adaptation paradigm (Grill-Spector et al., 1999) was used to test for BOLD decreases caused by immediate repetitions of the same identity at either the HSF or LSF bands, or in both, within hybrid stimuli. A given SF-filtered face could either be repeated (maximum 6 times; Lr, Hr for LSF, HSF repetition respectively) or changed (maximum 6 times; Ld, Hd for LSF, HSF differing, respectively). The number of repeated events per condition varied to disguise the experimental structure and hence control for possible attention or strategic effects that might confound the interpretation. Stimuli were presented in an event related manner with each stimulus shown for 500ms with an SOA of 1250ms.

Attention to either HSF or LSF was systematically manipulated across blocks, using an explicit cue that instructed subjects to attend only to one SF range in which inverted inner face targets could occasionally appear (the letter 'L' signalled attention to HSF, described to subjects as the components that looked more like "line-drawings" faces, whereas the letter 'B' signalled attention to LSF, described to subjects as the "blurred" faces). The cue was presented during each ISI. Subjects were instructed to maintain fixation, to attend the SF range indicated by the cue, and to report any inverted-face that appeared as quickly and accurately as possible with a button press. A target –inverted inner features- always appeared in the SF band that was cued. This was done to insure that subjects' attention was constantly directed to a given SF. In each 'attention' block, about 80 hybrid faces were presented; with about 15% target stimuli, 30 upright neutral faces (constituting the experimental events), plus filler items (40 with neutral and non neutral expression, see footnote 1). The fillers were included to dilute and thus disguise the repetition manipulation. There were 4 blocks per attention condition (total 8 blocks), with 6-9s of a blank screen with just a fixation point presented centrally between each of the different

attention blocks. Each block started with the presentation of 5 fillers to avoid confounds due to task switching. The final design had three factors (**Fig. 6.1c**): 2 (Attention, HSF, LSF) by 2 (LSF repetition: Lr, Ld) by 2 (HSF repetition: Hr, Hd). Note that visual stimuli always contained both HSF and LSF information and sensitivity was tested by comparing responses separately within each SF range (e.g. sensitivity to HSF was tested by comparing Hd vs. Hr).

Prior to scanning, subjects practiced the task. After the fMRI experiment, they were debriefed and asked whether they had noticed any structure in the order in which stimuli appeared. None reported noticing repetition, presumably thanks to the fillers and the varied number of events per condition.

**Imaging.** A Siemens 1.5T Sonata system (Siemens, Erlangen, Germany) was used to acquire 26 oblique slices, 3 mm thickness, with a 1.5mm gap and an in-plane resolution of  $3 \times 3 \times 4.5 \text{ mm}^3$ , with  $64 \times 64 / 900 / 50 \text{ msec} / 2340 \text{ sec}$  (matrix/ FA/ TE/ TR) see **Chapter 2** for more details.

**Data Analysis.** Pre-processing included spatial realignment, normalization and smoothing (see **Chapter 2** for more details).

The first-level design matrix included eight regressors each depicting the onset of each event for the eight experimental conditions (recall the  $2 \times 2 \times 2$  design), with fillers and targets modelled separately. The regressors were convolved with the canonical HRF (Friston et al., 2003). In addition, the 6 movement parameters obtained from the realignment procedure were included in the design matrix, to correct for possible artefacts due to head movement.

Consistent effects across subjects (second level analysis, random effects model, Friston et al., 1999) were tested using the resultant contrast images from the first level in one-sample t-tests. Conjunction analyses (Friston et al., 1999) were also used in order to test for cortical regions sensitive to repetition in both high and low SF and to test for cortical regions that showed reduced activation for a specific SF repetition and an increase when attending to that particular SF range. These conjunction



analyses were calculated using repeated-measure ANOVAs with correction for violation of sphericity at the second level.

A further analysis was performed on the maxima activation in occipito-temporal cortices obtained in the above analysis in SPM in order to establish functional-anatomical dissociations. Using repeated-measure ANOVAs in SPSS a region-by-condition interaction, with 2 (regions) by 2 (HSF: Hr, Hd) by 2 (LSF: Lr, Ld) factors collapsed across the attention factor was computed. All reported results were Greenhouse-Geisser corrected to account for possible violation of sphericity.

Finally, to assess selectivity of SF repetition decreases, an '*adaptation ratio*' was calculated for each SF band by dividing the estimated response for the SF repeated condition by the corresponding response for the non-repeated conditions, taken from peaks activation obtained from the SPM second level analysis (see above), separately for each subject (similar to Grill-Spector et al., 1999; Rotshtein et al., 2001). Note that a higher ratio indicates less repetition-related decrease. Paired t-tests were used to compare *adaptation ratios* for the two SF ranges within each region.

## 6.3 RESULTS

There was no significant difference in subjects' performance in detecting LSF compared to HSF inverted-face targets. Correct responses were  $92.41 \pm 2.0\%$  and  $91.5 \pm 9.4\%$  and reaction times were  $637 \pm 71.3\text{sec}$  and  $632 \pm 67.1\text{sec}$  for the LSF and HSF attention conditions, respectively. This suggests that any differences between the two SF attention conditions can not be explained by differences of task demands and attention load.

The focus of this thesis is in dissociating processes within occipito-temporal cortices (see **Chapter 1**). Therefore I concentrated on activations from these regions, but for completeness, in the tables I reported all regions showing significant effects above threshold of  $P < 0.001$  uncorrected. No above threshold interactions between attention and SF repetition or between LSF and HSF repetition were observed in occipito-temporal cortices. Therefore, I only reported main effects and conjunctions.

Sensitivity to HSF information in a face was tested by comparing the conditions where this information repeated to those where it differed (i.e. Hd > Hr). Reduced fMRI signal for HSF repetition, independent of LSF repetition was observed in the right IOG (**Fig. 6.2a**) and the left inferior temporal gyrus (ITG; **Table 6.1a**). In both these regions, decreases for HSF were significantly larger than that of LSF face repetition (**Table 6.1b**). The magnitudes of these decreases were quantified by calculating their adaptation ratios. The right IOG showed smaller adaptation ratio (indicating greater reduction in signal) for the repetition of HSF compared to LSF faces ( $t_{13} = 2.36$ ,  $P < 0.05$ ; **Fig. 6.2a**), whereas the left ITG showed no significant difference in adaptation ratios for different SFs ( $t_{13} = 0.13$ ,  $P = 0.9$ ). Therefore, the right IOG is suggested to be the only region that showed a clear preferential response to HSF relative to LSF information in faces, while the left ITG showed only a tendency. Selective attention to HSF faces did not affect right IOG activity, but affected left ITG activity. This is demonstrated by a conjunction analysis that tested for areas that showed increased activation with explicit attention to HSF and decreased activation for repetition of HSF faces (**Table 6.1c**).

**Table 6.1: High spatial frequency (HSF) effects**

Anatomical Description		Z score	MNI		
			x	y	z
=====					
A.	<b>Main effect of HSF repetition:</b> <i>HSF-diff &gt; HSF-rep</i>				
IOG	R	3.64	36	-84	-9
IOG	R	3.28	48	-66	-12
ITG	L	3.45	42	-24	-27
SFG	M	3.73	3	3	69
<b>B. Main effect HSF repetition &gt; LSF repetition:</b> <i>(HSF-diff &gt; HSF-rep) &gt; (LSF-diff &gt; LSF-rep)</i>					
IOG	R	2.61	54	-63	-9
IOG	R	2.53	33	-87	-9
ITG	L	3.52	-54	-24	-27
SFG	M	3.48	3	6	69
ACG	L	3.89	-15	27	-6
<b>C. Conjunction HSF repetition &amp; HSF attention:</b> <i>(HSF-diff &gt; HSF-rep) &amp; (attention HSF &gt; LSF)</i>					
ITG	L	3.03	-42	-24	-27
<b>D. Main effect HSF Attention: HSF &gt; LSF</b>					
Non significant					

IOG: inferior occipital gyrus; ITG: Inferior temporal gyrus; SFG: superior frontal sulcus; aCG: anterior cingulate gyrus; M: middle; L: left; R: right hemisphere. Minimum T(26)=1.89 used for the conjunction analysis.

Conversely, reduced fMRI signal for repetition of LSF faces, independent of any HSF components of the hybrid stimuli, were found in bilateral MOG and in the right middle FFG (**Table 6.2a, Fig. 6.2b**). Only in the left MOG was reduced activation for LSF-repetition more pronounced than that for HSF-repetition (**Table 6.2b**), this was also evident as a difference in the adaptation ratios (left MOG:  $t_{13} = 2.26$ ,  $P < 0.05$ , **Fig. 6.2a**; right MOG:  $t_{13} = 0.866$ ,  $P = 0.4$ ; right FFG:  $t_{13} = 0.845$ ,  $P = 0.41$ ). Thus, the left MOG is the only region showing a clear preferential response for LSF relative to HSF information in faces, while the right MOG and the mid-FFG only showed a tendency to prefer LSF information. Selective attention to LSF increased activation in bilateral MOG and the right mid FFG. Similarly, a conjunction analysis revealed that the above foci that showed increased activation following LSF-attention overlapped with the region that showed decreased activation during repetition of LSF faces (**Tables 6.2c,d**).

**Table 6.2: Low spatial frequencies (LSF) effects**

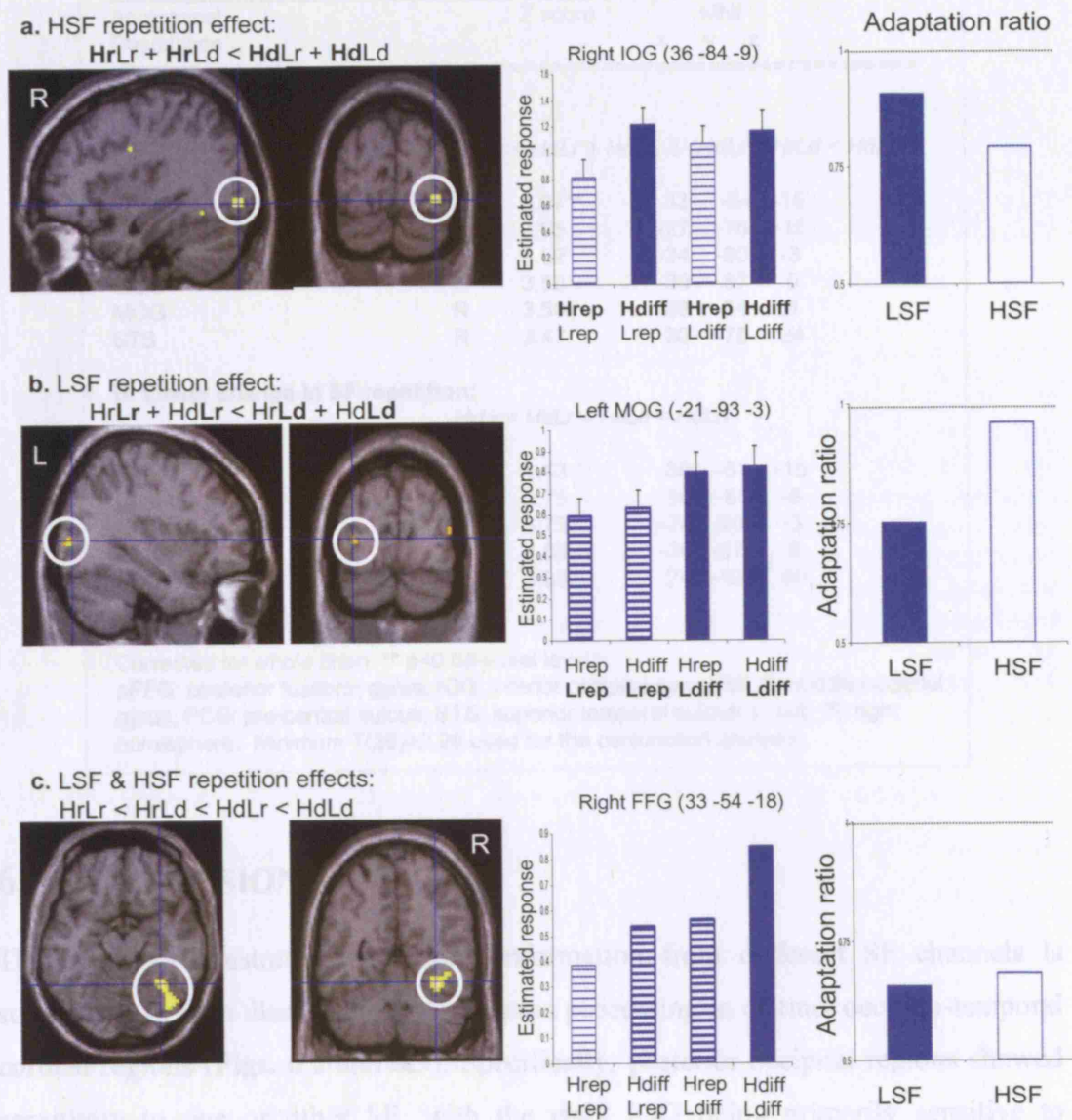
Anatomical Description	Z score	MNI		
		x	y	z
=====				
<b>A. Main effect of LSF repetition:</b>				
<i>LSF-diff &gt; LSF-rep</i>				
MOG L	4.05	-21	-93	-3
MOG L	3.64	-33	-87	3
MOG L	3.29	-39	-75	12
MOG R	3.40	30	-87	12
MOG R	3.25	45	-84	12
mFFGR	3.59	42	-51	-12
PCS R	4.36	24	-12	60
PCS L	3.34	-24	-12	54
IPS R	3.49	27	-72	33
<b>B. Main effect LSF repetition &gt; HSF repetition:</b>				
<i>(LSF-diff &gt; LSF-rep) &gt; (HSF-diff &gt; HSF-rep)</i>				
MOG L	3.24	-39	-75	9
<b>C. Conjunction LSF repetition &amp; LSF attention:</b>				
<i>(LSF-diff &gt; LSF-rep) &amp; (attention LSF &gt; HSF)</i>				
MOG L	5.11**	-36	-84	6
MOG R	4.55	33	-90	12
mFFGR	3.66	24	-57	-15
IPS R	4.52	27	-72	33
<b>D. Main effect LSF Attention: LSF &gt; HSF</b>				
MOG L	3.20	-39	-93	12
MOG R	3.11	39	-93	9
IFG R	4.15	60	-6	12
IPS R	3.94	27	-90	33
IPS L	3.42	-33	-72	21

Corrected for whole brain: \*\*  $p < 0.05$ -voxel level.

MOG: middle occipital gyrus; mFFG: middle fusiform gyrus; PCS: pre-central sulcus; IPS: intraparietal sulcus; IFG: inferior frontal gyrus; L: left; R: right hemisphere. Minimum  $T(26) = 2.43$  in the conjunction analysis.

Finally, reduced activation following repetition of either HSF or LSF (or both) was observed bi-laterally in the ventral cortical visual stream with a larger effect in the right posterior FFG (**Fig 6.2c, Table. 6.3**). This repetition sensitivity, common to both SF ranges, was revealed by a conjunction analysis, testing for regions showing decreased activation during the repetition of either of the two SFs ( $HdLd > HrLd + HdLr$ ) and increased activation for changes in either of the SFs ( $HrLr < HrLd + HdLr$ ). Interestingly, there was no significant interaction between repetition of LSF and of HSF faces in the right FFG ( $F_{1,13} = 0.657$ ,  $P = 0.4$ ) but only significant SF repetition effects (HSF:  $F_{1,13} = 12.1$ ,  $P < 0.005$ ; LSF:  $F_{1,13} = 18.6$ ,  $P < 0.001$ ). This suggests that in the context of the current experiment, SF information converged but did not interact in the right FFG. This was further demonstrated as a significant linear component in the pattern of activation of the right posterior FFG ( $F_{1,13} = 29.4$ ,  $P < 0.001$ ; see also **Table 3B** and **Fig. 6.2c**). In accordance with the above there was no significant difference in adaptation ratios of HSF and LSF faces ( $t_{13} = 0.851$ ,  $P = 0.4$ ).

The results suggest a possible functional-anatomical dissociation between the FFG, right IOG and left MOG. This dissociation was tested using a region-by-condition interaction with regions (IOG or MOG, FFG), LSF and HSF repetition conditions as factors. A differential response for LSF was observed for the right IOG and right FFG (interaction of region-by-LSF:  $F_{1,13} = 5.1$ ,  $P < 0.05$ ) where only the latter showed a reduced response to repetition of LSF faces. However, both regions show similar reductions in their response for repetition of HSF (main effect HSF:  $F_{1,13} = 23$ ,  $P < 0.001$ ; with no interaction of region-by-HSF:  $F_{1,13} = 0.2$ ,  $P = 0.6$ ). Conversely, the right FFG differed significantly from the left MOG in response to HSF repetitions (interaction of region-by-HSF:  $F_{1,13} = 7.1$ ,  $P < 0.05$ ), demonstrating that only the former response was modulated by repetition of HSF faces, while both regions showed similar reductions in their response to LSF repetition (main effect LSF:  $F_{1,13} = 36$ ,  $P < 0.001$ ; with no interaction of region-by-LSF:  $F_{1,13} = 0.48$ ,  $P = 0.5$ ). This confirms that the right posterior FFG as opposed to right IOG and left MOG, showed no selective repetition decrease for one or the other SF; instead this region adapted equally to information from both SF bands, while the right IOG sensitivity was selective to HSF information and the left MOG was selective to LSF information.



**Figure 6.2: Spatial frequency specific effects**

On the left, statistical parametric maps depicting regions sensitive to HSF (a) LSF (b) and both (c) information in a face, across subjects (threshold  $P < 0.001$ , uncorrected), overlaid on coronal and sagittal T1 images of one subject. In the middle, the histograms show the averaged estimated response for four conditions (collapsed across attention) taken from the maxima voxel marked with blue crosshairs and a white circle, for which coordinates are given above each histogram (in MNI space). On the right, averaged adaptation ratio across subjects for the same maxima voxels, calculated by dividing the 'repetition' by the 'different' conditions, performed separately for each SF. The higher the bar, the less repetition decrease was observed (see Methods). Acronyms: LSF/HSF: low/high spatial frequency; rep (r): repeat; diff (d): different; IOG: inferior occipital gyrus; MOG: middle occipital gyrus; FFG: fusiform gyrus; L: left; R: right.

**Table 6.3: Convergence of HSF & LSF repetition effects**

Anatomical Description	Z score		MNI		
			x	y	z
=====					
<b>A. Conjunction HSF &amp; LSF:</b>					
<i>(HrLr &lt; HdLr + HrLd) &amp; (HdLr + HrLd &lt; HdLd)</i>					
pFFG	R	5.07**	33	-54	-15
IOG	L	3.65	-27	-78	-15
MOG	L	3.52	-24	-90	-3
MOG	L	3.50	-39	-87	0
MOG	R	3.50	39	-84	6
STS	R	3.47	30	-75	24
<b>B. Linear change in SF repetition:</b>					
<i>HrLr &lt; HdLr &lt; HrLd &lt; HdLd</i>					
pFFG	R	4.43	36	-51	-15
IOG	R	3.75	36	-81	-6
IOG	L	3.75	-24	-90	-3
MOG	L	3.63	-36	-87	6
PCS	R	3.88	24	-12	60

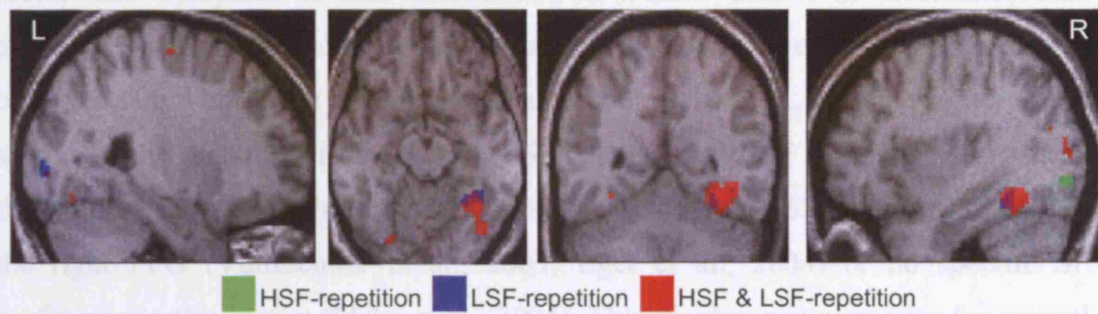
Corrected for whole brain: \*\* p<0.05-voxel level.

pFFG: posterior fusiform gyrus; IOG: inferior occipital gyrus; MOG: middle occipital gyrus; PCS: pre-central sulcus; STS: superior temporal sulcus; L: left; R: right hemisphere. Minimum T(26)=2.26 used for the conjunction analysis.

## 6.4 DISCUSSION

This study demonstrated that visual information from different SF channels is susceptible to both dissociable and common processing in distinct occipito-temporal cortical regions (**Figs. 6.2** and **6.3**). Specifically, posterior occipital regions showed sensitivity to one or other SF, with the right IOG being primarily sensitive to repetition of high SF information (**Figs. 6.2a** and **6.3, Table 6.1**) and the left MOG being sensitive to repetition of low SF information of a face (**Figs. 6.2b** and **6.3, Table 6.2**). By contrast, a more anterior region, the right FFG showed sensitivity to repetition of either high or low SFs (**Figs. 6.2c** and **6.3, Table 6.2**). Two additional anterior foci along the ventral stream showed a degree of preferential responding to SF, as indicated by both the repetition and the attention manipulation, with the right mid-FFG being sensitive to LSF and the left ITG responding to HSF information from a face. These results show that within occipital-temporal cortices different regions are involved in processing different SF information from a face suggesting they have a different role in processing faces.





**Figure 6.3: Overview of SF effects**

The effects of interest are overlaid on a single subject T1 image ( $P < 0.001$ , uncorrected). Green depicts the region showing sensitivity to HSF (i.e.  $H_d > H_r$ , collapsed across LSF and attention factors). Blue depicts the regions showing sensitivity to LSF information (i.e.  $L_d > L_r$ , collapsed across HSF and attention factors). Red depicts regions showing sensitivity to either HSF or LSF calculated by a conjunction contrast, whereby change in either and in both types of SF information produced differential responding compared to that of repetition in either and in both SF (see **Table 6.3A**, and **6.3 Results**). Note that posterior regions showing sensitivity to either HSF (green) or LSF (blue), while the posterior FFG shows sensitivity to both (red) with more anterior parts of it showing some preferential responding to LSF (blue).

The dissociation of SF information reported here in posterior occipital cortices accords with previous findings that demonstrate more activation for HSF compared to LSF faces in the right IOG (Vuilleumier et al., 2003; Eger et al., 2004) and a larger response to LSF compared to HSF faces more dorsally in bilateral parieto-occipital cortex (Vuilleumier et al., 2003). However others have reported increased activation for LSF faces in more mid-posterior cortices i.e. the calcarine sulcus rather than in more dorsal regions (Eger et al., 2004) as observed here.

It is worthwhile noting that this functional dissociation may reflect a more general organization of posterior occipital cortices and hence may not be limited to face processing. As described above one branch of the magno-cellular pathways, (associated with low SF) projects to the dorsal occipital cortex, specifically to a region involved in processing motion information i.e. MT/V5 (Shipp et al., 1995), which is in the vicinity of the left MOG, with the latter being involved in the processing of LSF information, as suggested here.

Some tendencies for preferential processing of SF information were also observed in more anterior regions along the ventral stream. The left ITG showed a tendency to

prefer HSF compared to LSF information in a face. This is in accordance with previous studies where larger responding to HSF compared to LSF faces was observed in the left ITG (Vuilluermier et al., 2003; Idaka et al., 2004). The right FFG showed some preferential tendency to LSF compared to HSF information in a face; this contradicts others who showed a stronger response to HSF compared to LSF in the right FFG (Vuilluermier et al., 2003; Eger et al., 2004) or no specific SF preference in this region (Idaka et al., 2004). This discrepancy may arise for several reasons. The first relates to the different ways in which SF regional responses were determined, here as repetition decreases, while in other studies as the amplitude of response to a specific SF band (Vuilluermier et al., 2003; Eger et al., 2004; Idaka et al., 2004). Second, the stimuli used here were different; recall that I used a hybrid face, presenting simultaneous information for both HSF and LSF, while in the other studies only one SF band was presented at a time. Thirdly, these discrepancies can arise due to differences in task requirements, here the detection of an inverted face while others used gender decision tasks (Vuilluermier et al., 2003; Eger et al., 2004).

Interestingly, dissociable effects were observed even though repetition was manipulated only on a selection of the visual stimuli, either on one of the low or high SF components of the hybrid face. This supports the idea that HSF and LSF information are processed independently, even when presented within a single image, as is the case in natural images.

Importantly, besides dissociable LSF and HSF responses in posterior occipital cortices, a distinctive pattern with common sensitivity to a broad SF range in faces was found in the right FFG. This region showed a different profile compared to either right IOG or left MOG, as it did not show any preferred SF information in faces. Note, however, that the current study was not designed to test for integration of SF processes but for dissociation between them. Therefore, it is only demonstrated that right FFG sensitivity was for repetition of both SFs in an additive fashion with no interaction. Others have shown that right FFG can also integrate SF information (Vuilluermier et al., 2003; Eger et al., 2004).

The results suggest that selective attention and stimulus-repetition provide orthogonal measures of sensitivity to different properties of visual stimuli. BOLD



responses in bilateral MOG decreased for events in which LSF faces were repeated and increased during blocks in which attention was directed to LSF faces (**Table 6.2**). On the other hand, right IOG sensitivity to HSF information in faces was observed only as a decreased signal for HSF repetition but not as increased activation following explicit attention to HSF faces. The lack of an HSF attention effect in the right IOG cannot be ascribed to task confounds as no such differences were observed in subjects' behaviour. Moreover, increased activation for HSF attention conditions was observed in other brain regions that showed sensitivity to the HSF repetition manipulation (i.e. the left ITG). One possible explanation for the lack of a HSF attention effect in posterior occipital cortices might relate to the observation that parvo-cellular responses are not modulated by attention as opposed to magno-cellular responses (Di Russo et al., 2001); recall that parvo-cellular pathways convey high SF information to the cortex and therefore it is not surprising that early visual regions that are receiving parvo-cellular inputs were not modulated by attention.

In conclusion, the present results support a differential cognitive role for SF in face processing. The data suggests that processes in the posterior occipital cortex, presumably reflecting early face processing separate high and low SF information in a face. This dissociation provides a plausible neuronal infrastructure that can support hypotheses such as the *coarse-to-fine*, and the *flexible usage* of SF (**see 6.1, Introduction**). Moreover the findings suggest that in more anterior regions (FFG) there is a convergence between SF information from faces, suggesting that it reflects higher processes within the hierarchal model compared to more posterior regions where information is segregated (i.e. IOG, MOG). However, SF preferential responding in more anterior regions need to be further explored. In the next chapter I test whether similar dissociations are revealed if information from a face is divided according to cognitive definitions.

# CHAPTER 7:

## PROCESSING FEATURAL AND

## CONFIGURAL INFORMATION FROM

## A FACE

---

### 7.1 INTRODUCTION

#### *7.1.1 Defining features and configuration*

Faces contain different types of information. These different types are associated with different cognitive processes, and hence might involve different brain regions. It is suggested that the elementary components in a face are its features; the shape of an eye, its colour, the shape of a nose etc. These are also known as ‘first order features’ (Rhodes, 1988) or ‘face components’ (Sergent, 1984). A face also contains configural information (Rhodes, 1988; Sergent, 1984, Maurer, 2002). Three types of configural processes have been defined (Maurer, 2002): First are processes of first-order spatial relations of facial features (1<sup>st</sup>-conf). 1<sup>st</sup> order relations are fixed across all faces as Humpty Dumpty points out, and are termed the canonical configuration. Essentially 1<sup>st</sup>-conf is what allows an object to be perceived as a face, e.g. eyes above nose and below forehead. Second, holistic processes of a face use gestalt grouping of facial features in which all features are processed as a group and not separately (Farah et al., 1998). Third are processes of second-order spatial relations (2<sup>nd</sup>-conf) between the different features, i.e. distance between the eyes, distance between the mouth and the nose, distance between the eye brows and the hairline etc. There have

been several hypotheses regarding the differential role of featural and configural information in face processing and these are described next.

### ***7.1.2 The configural approach for face processing***

The configural approach to face processing argues that faces as opposed to objects are processed using configural information, specifically of the second order information utilised in a holistic way (cf. Diamond and Carey, 1986, Farah et al., 1998).

#### **7.1.2a Cognitive research**

In psychology research stemming from a configural approach to face processing relies on two main paradigms: The *face inversion effect* and the *face context effect*.

*The face inversion effect* - This intriguing phenomenon described first by Yin (1969) and followed by a large body of research (see Valentine, 1988 for review), demonstrates that inverting a face impairs the performances of healthy adults in face perception, recognition and identification tasks, despite that the inversion of other objects does not affect performances in the same way (Yin, 1969). A related phenomenon is the “Thatcher illusion” (Thompson 1980), whereby inverting only inner features of the face (eyes, mouth, nose) but preserving canonical first order relations results in a grotesque appearing face, however this grotesque effect is significantly attenuated if the ‘thatcherized’ face is viewed upside down (Thomson, 1980; Rotshtein et al., 2001).

Failures in processing inverted faces are attributed to disruption of holistic (Young et al., 1987; Farah et al., 1998) and 2<sup>nd</sup>-conf processes (de Gelder et al., 2000; Mondloch et al., 2002). It has been suggested that the inversion of a face violates the canonical 1<sup>st</sup>-conf<sup>2</sup> and therefore forces subjects to use a different strategy to process a face, specifically to rely more on featural information (Tanaka and Farah, 1993). In support of this latter hypothesis, it is demonstrated that the face inversion effect is

---

<sup>2</sup> Are canonical 1<sup>st</sup>-conf violated by inversion? A simple mental rotation can restore the canonical configuration. An inversion of a face does not affect the spatial relation between its features. Furthermore, single cells do not show differential sensitivity to face orientation but do show sensitivity to violation of 1<sup>st</sup>-conf by jumbling the features (see below), suggesting that face inversion is not simply violation of 1<sup>st</sup>-conf.

attenuated if a face is studied on a feature by feature basis using the ‘feature explosion’ manipulation (Farah et al., 1995). However, only a few studies have directly tested the assumptions behind the inversion manipulation and the few that have suggest that inverting a face impairs both featural and configural processing (Yovel and Kanwisher, 2005). One aim of the current study was to re-visit this assumption and directly test the effect of violation of 1<sup>st</sup>-conf on featural and 2<sup>nd</sup>-conf processing.

*The face context effect* - The face context effect is argued to reflect holistic face processing (Maurer et al., 2002; Farah et al., 1998). It has been demonstrated that the ability to match features is enhanced if the features are presented in the context of a face in contrast to the features being presented on their own (Honma et al., 1976; de Gelder and Rouw, 2000; Bounsten and Humphreys, 2002). Identifying a single feature is also shown to be facilitated by the context of a whole face (Tanaka and Farah, 1993) and identification is impaired if two different face halves (e.g. half Bush, half Clinton) are merged to form one, compared to when they are spatially shifted (Young et al., 1987). More so, subjects are better at identifying a single feature (e.g. this is John’s nose) if it was learned in the context of an upright face compared to an inverted face, or jumble-feature face; this advantage was specific to faces and was not observed for houses (Tanaka and Farah, 1993).

### **7.1.2b Neuropsychological research**

Neuropsychological research using the above framework suggests that prosopagnosia is associated with impaired configural processes, specifically of the holistic and 2<sup>nd</sup>-conf types (de Gelder, 2003; Joubert, 2003, Boutsen, 2002) but featural processing (de Gelder et al., 2003, Boutsen et al., 2002) and 1<sup>st</sup>-conf processing (Duchaine, 2000; Le, 2003, de Gelder, 1998, Bobes, 2003) are still intact. This hypothesis relies on findings from three paradigms.

*The inversion inverted face effect* – Surprisingly, some prosopagnosia patients’ were not affected by inversion while others even improved their performances on perceptual matching tasks (Farah et al., 1995; de Gelder et al., 1998). In some patients, the inversion inverted effect was not restricted to faces and was observed for other types of objects (de Gelder and Rouw, 2000), supporting the idea that these

patients have a general problem in processing configural information and their deficit is not face specific. However, not all prosopagnosic patients show an *inversion inverted* face effect (de Gelder and Rouw, 2000), suggesting again that prosopagnosia is a heterogeneous phenomena.

*The face context effect* – Some prosopagnosic patients do not show a face-context effect (Perrett et al., 1988) and in some cases features are processed even better without the face context- an *inversion* of the face-context effect (de Gelder et al., 2003, Boutsen et al., 2002). In some patients this *inversion* of the context effect is observed for houses as well as for faces (de Gelder and Rouw, 2000).

Processing of *second-order spatial relations* (2<sup>nd</sup>-conf) within a face is tested as subjects' ability to detect such a change, in comparison to their ability to detect a change in features (Maurer et al., 2002). The few prosopagnosia patients that have been tested using such a stimuli manipulation in a matching task were found to be more impaired in detecting a 2<sup>nd</sup>-conf change than a feature change (Joubert et al., 2003; Barton et al., 2002, 2003).

These empirical findings suggest that while some prosopagnosic patients are impaired in configural processing, it is not the case with all; thus, undermining the hypothesis that face processing is based strictly on configural information.

### 7.1.2c Humans as face experts

An associated hypothesis to the role of configural information in face processing is the expertise hypothesis. Humans are experts in recognizing and identifying faces. It has being argued that as face experts, we have developed special and more efficient strategies to process them (Carey 1992; Guathier and Nelson, 2001). These strategies generate heuristics based on a-priori knowledge regarding faces (such as the knowledge of the canonical 1<sup>st</sup>-conf of a face; recall the *fiducial point* in the *Lattice* model, Biederman and Kalocsai, 1997). It has been suggested that these heuristics mostly rely on configural rather than on featural processing. Humpty-Dumpty complains (see p.139) that all faces are similar (i.e. same 1<sup>st</sup>-conf): therefore he cannot tell them apart. Humpty-Dumpty is obviously not an expert in processing human faces as opposed to Alice. To become an expert in faces one needs to learn to

identify a particular face from the relatively homogenous category of faces (e.g. 'this is Chloe's face, and not Joy's'). Object classification on the other hand, does not require identifying a particular example of a category e.g. 'this is the chair of my grandma' but rather 'this is an office chair, and not a table, or an orange'. Note that even when classification of subcategories is tested, it is usually not at the level of a particular individual sample, e.g. "this is a Cocker-Spaniel and not a Poodle" (Diamond and Carey, 1986) as opposed to "this is Uta's poodle". The expertise hypothesis suggests that subordinate level discrimination is developed to rely on holistic and 2<sup>nd</sup>-conf information as they are more reliable and efficient processes, while discriminating between categories can be achieved based on featural information; for example if it has one leg and four wheels it is probably an office chair.

Developmental research supports the expertise hypothesis suggesting that face processing qualitatively changes with development, from relying on features to involving holistic and configural processing, for example, children (younger than 10y) do not show the face inversion effect (Carey and Diamond, 1977; De Haan et al., 2000). The role of experience has been demonstrated for dog experts' that show a *dog inversion* effect. This effect was not observed for non-dog-experts (Diamond and Carey, 1986).

In line with the expertise hypothesis prosopagnosia has been suggested to reflect a within category discrimination deficit. Supporting the proposition that such discrimination deficit can emerge, is a single case farmer lost his ability to identify his cows with the ability to identify faces (Bornstein et al., 1969). Similarly some prosopagnostic patients are also impaired in the subordinate discrimination of non-faces (Gauthier et al., 1999). However, opposite striking examples exist as well. A patient that learned to identify his sheep by their faces although he had lost his ability to identify human faces (McNeil and Warrington, 1993), or a patient who lost his ability to recognize faces but maintained his expertise in recognizing particular craftsman's vases (Semenza et al., 2003). These cases suggest that not all prosopagnostic conditions can be explained solely on the idea of within category deficits, or deficit in expertise skills.

### **7.1.3 Electrophysiology recordings in monkeys**

Three different types of cell response to faces were observed in macaques' IT (Perrett et al., 1992): *feature specific*, *view-angle selective* and *view-general face cells*.

*Face feature specific cells* prefer a specific feature of a face, such as eyes, mouth, hair etc. and showed reduced responding when this feature was not presented. Some of these cells are sensitive to 1<sup>st</sup>-conf of these features, and do not respond if the canonical configuration is violated by jumbling the features (Perrett et al., 1986).

*View-angle selective cells* modulate their responses depending on the viewing angle of a face, i.e. front-view, profile, back-view, tilted up, or tilted down. Some cells respond maximally to “profile”, while others to “front-view” of a face. These cells reduce their response to half if the head is presented at 3/4 profile. These cells also generalized across different size and location on the retina, different lightening conditions and different head orientations (in 2D plain, i.e. inversion of face). Similarly some cells show a preferred response for a particular feature within a face and/or to the 1<sup>st</sup>-conf (Perrett et al., 1986).

Some *view-angle selective cells* show a preferential response for a specific individual, such that they respond more strongly to a particular identity compared to another. However, these cells still have a larger response to other identities when compared with non-face objects. Their preferential response for a specific identity is generalized across viewing conditions, as described above, and also across different expressions, but not across different angles-of-views. This sensitivity for a preferred individual-face might be attributed to a particular feature in a face or to a typified configuration of features (Perrett et al., 1986).

*View-general face cells* respond to all presented angles of a face. 10% of cells responding to faces had a preferred identity to which they responded more strongly compared to other identities. They are assumed to receive information from all the previous cells and to be at the end of hierarchical processing of face identity (Perrett et al., 1986).

Recordings from the temporal cortex of sheep showed similar results (Kendrick et al., 1991). Small populations of cells responded (latencies less than 180msec) to pictures of human and animal faces, preferring frontal views and direct eye gaze. Other cells were sensitive to different aspects of a face; for example, the presence and length of horns, whether it was con-specific, whether a sheep face was familiar or selectively responding to human and dog faces (Kendrick et al., 1991).

The above findings suggest that face selective neurons encode both featural and configural information, and not just configural information as argued by the face configural approach.

#### ***7.1.4 Neuroimaging studies in human***

Electrophysiological studies demonstrate that the N170 reflects the encoding of information that relates to face orientation (Eimer 2000a) and to view angle (Eimer 2000b). This component is thus suggested to reflect early configural processes of faces (Bentin and Deouell, 2000 and Eimer 2000b). However, others have shown that the N170 is sensitive to facial features, in particular to the eyes (Sagiv and Bentin, 2001; Smith et al., 2004). Here it is suggested that the early face component reflects featural rather than configural related processes.

Using fMRI, a posterior-anterior gradient is demonstrated (Lerner et al., 2001), with posterior occipital cortices processing features that are not organized in canonical 1<sup>st</sup>-conf while the more anterior ventral regions show increased sensitivity to canonical 1<sup>st</sup>-conf (Lerner et al., 2001). Using PET hemispheric dissociation was demonstrated with featural processing in left FFA (i.e. functionally defined face fusiform gyrus) and configural processing in right FFA (Rossion et al., 2000). However, a recently published study did not report any differences between featural and 2<sup>nd</sup>-conf processes in FFA (Yovel and Kanwisher, 2004).

Intriguingly, the neuroimaging studies in humans as well as the electrophysiological recordings in monkeys suggest that both features and configural information are involved in face processing. This contracts the dominant hypothesis drawn from cognitive psychological and neuropsychological literature that argues in favour of configural information in face processing. This inconsistency might be partly related



to over-interpretation of the paradigms used, especially of the face inversion paradigm (Maurer et al., 2002). Other sources of this inconsistency might be due to the different tasks and stimuli used to investigate these processes in imaging and behaviour.

The aim of the following study was to test the differential role of features and 2<sup>nd</sup>-conf information in face processing using the same experimental design for measuring behaviour and brain responses. Specifically, the behavioural study focused on the processes that underlie face individuation (i.e. distinguishing between faces) and their affect on face recognition. Using a pair repetition paradigm (Chapter 5), either features and/or 2<sup>nd</sup>-conf of faces could be repeated or changed along consequently presented faces. These changes appeared in a context of canonical and non-canonical 1<sup>st</sup>-conf (see **Fig 7.1**). Importantly, in order to test for the relative contribution of featural 2<sup>nd</sup>-conf information to face processing in an ecologically plausible context, I used the natural variability of these two types of information in human individuals; thus stimuli were generated using featural and 2<sup>nd</sup>-conf information both taken from photographs of real individuals.

The first experiment (**sec. 7.2**) tested subjects' perceptual sensitivity to these changes, using an identity discrimination task. Two questions were addressed. The first relates to the relative contribution of featural and 2<sup>nd</sup>-conf information to face individuation. The second relates to the effect of 1<sup>st</sup>-conf on the processing of features and 2<sup>nd</sup>-conf. The fMRI experiment that follows (**sec. 7.3**) tested whether featural and configural information processes can be dissociated anatomically, and whether individual differences observed in the behavioural experiment are reflected in subjects' brain responses. Finally, I tested whether individual differences in subjects' sensitivity to featural and 2<sup>nd</sup>-conf change predicted their face recognition ability (**sec. 7.4**).

## 7.2 IDENTITY DISCRIMINATION EXPERIMENT – BEHAVIOUR WORK

### 7.2.1 Method

**Subjects.** 32 healthy volunteers participated (18 females, mean age 26, range 19-51y, 12 right handed) in the identity discrimination experiment. One subject failed to correctly use the response buttons and was excluded from analysis. All volunteers had normal vision and no concurrent or past neurological or psychiatric history. Informed consent was obtained according to procedures approved by the Joint Ethics Committee of the National Hospital for Neurology and Neurosurgery (NHNN) and Institute of Neurology (ION), London.

**Stimuli.** The initial stimuli set compromised 30 achromatic front view faces with neutral expressions taken from the Karolinska Directed Emotional Faces set (KDEF, Lundqvist, et al., 1998). Four rectangles of fixed size were used to choose the four basic features from each face (i.e. mouth, nose, two eyes + eyebrows; see **Fig. 7.1a**). The content of these rectangles was defined as the facial features, while the spatial relations between these rectangles were defined as 2<sup>nd</sup>-conf. A blank face with skin colour texture (see **Fig. 7.1a**) and unisex outline features (e.g. hair style, ears, chin contours etc.) served as a template image and the feature-rectangles were overlaid on it. A pilot study confirmed that different combinations of features and 2<sup>nd</sup>-conf, even when taken from different faces, did not affect face 'realness': in other words subjects were not reliably able to relate 2<sup>nd</sup>-conf to its original features (see **Fig. 7.1b** for examples of the stimuli used). 1<sup>st</sup>-conf was manipulated by inverting the inner feature-rectangles within the template.

**Experimental procedure.** The experiment had a 2 (features repetition) by 2 (2<sup>nd</sup>-conf repetition) by 2 (1<sup>st</sup>-conf) factorial design. There were four pair types that could either be presented in canonical 1<sup>st</sup>-conf (i.e. upright inner features) or in non-canonical 1<sup>st</sup>-conf (i.e. inverted inner features; **Fig. 7.1a**). Repetition was manipulated in the second face in a pair that could either have the same features and same 2<sup>nd</sup>-conf; same features and different 2<sup>nd</sup>-conf; different features and same 2<sup>nd</sup>-conf or different features and different 2<sup>nd</sup>-conf from the preceding face. This

resulted in four repetition types for each face (60 different pairs for each 1<sup>st</sup>-conf). Note that for a given inner face context (i.e. 1<sup>st</sup>-conf) the faces that were first in a pair were identical across all conditions and only the second face varied. Across subjects, the faces that were first in a pair were randomly assigned.

The subjects' task was to judge whether two faces had the same or different identities. They were asked to respond as quickly and accurately as possible. In order to make the pair structure explicit, the trial started with an empty circle presented for 500ms, each face was then presented for 500ms, with a 500ms interval between the two faces. The trial ended with a 1000ms fixation point, giving a total of 3000ms SOA. Each face-pair was presented twice, with a total of 30 trials per condition. The order of the trials was randomized.

This study was run on two occasions, once following the fMRI experiment specified below ( $n = 13$ ) thus subjects saw all the faces during the fMRI experiment, before performing the identity discrimination task. For replication purposes a second cohort of subjects was run without the subjects seeing the stimuli before hand ( $n = 18$ ).

**Data analysis.** Data were analyzed using Matlab6.0 and SPSS11.0. Results for 'different' responses are presented (**Fig. 7.2**) as a proportion of the total number of pairs per condition (i.e. out of 30). Reaction times for the 'different' responses were also analyzed. All reported results are Greenhouse-Geisser corrected for possible violation of sphericity.

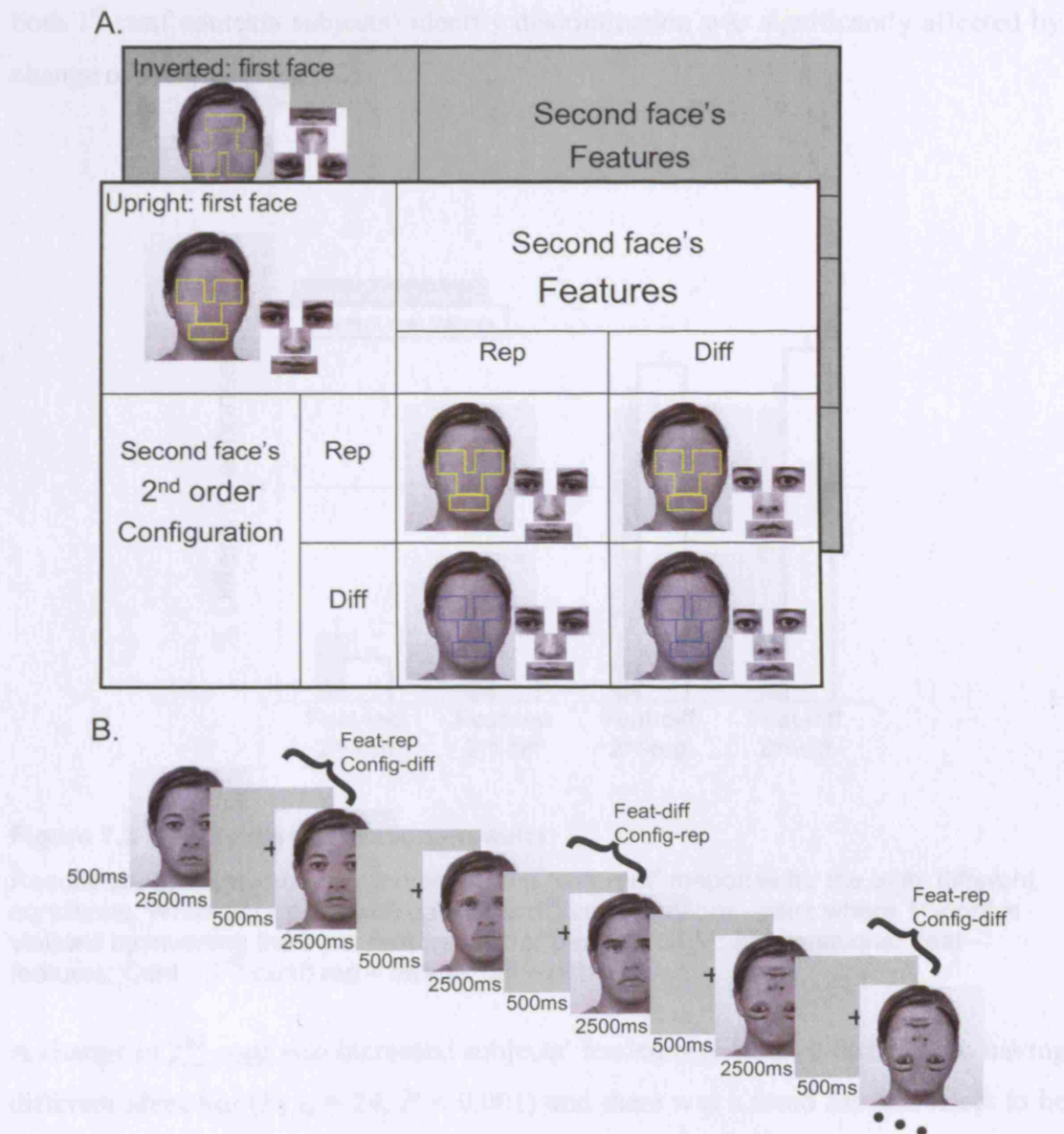
#### **7.2.2 Results & Discussion**

There were no significant difference between the two groups of subjects, hence no effect of prior exposure to the faces or the level of familiarity with the faces. Hence the results were collapsed across all subjects and presented together (**Fig. 7.2**).

As expected, subjects judged more face-pairs as having different identities in canonical compared to non-canonical 1<sup>st</sup>-conf contexts ( $F_{1,30} = 4.4$ ,  $P < 0.05$ , **Fig. 7.2**). In addition, reaction times for canonical pairs (937msec) were faster compared to non-canonical pairs (905msec,  $F_{1,19} = 5.5$ ,  $P < 0.05$ ). This suggests that violating

1<sup>st</sup>-conf affects sensitivity to the identity change and that generally processing non-canonical face is less efficient compared to canonical.

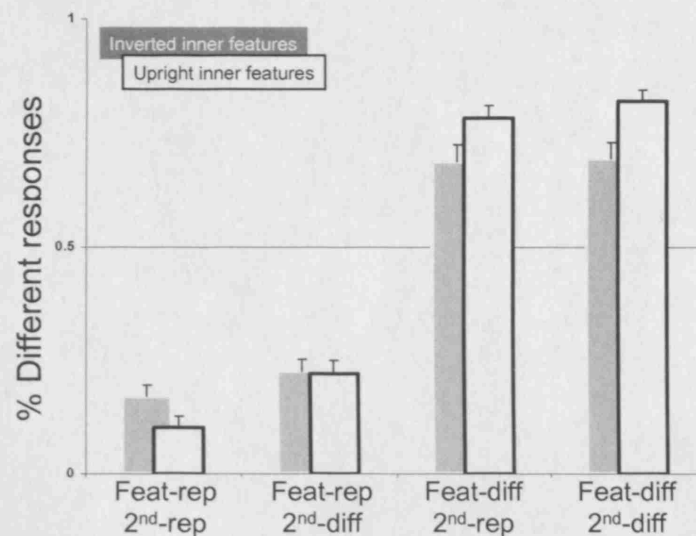
way-orientation feature (by-orientation,  $F(2, 20), p < 0.001$ ). However, note that in both conditions subjects' identity discrimination was significantly affected by changes in



**Figure 7.1 Experimental design**

**A.** The experiment had a 2 (features repetition) by 2 (2<sup>nd</sup>-conf repetition) by 2 (1<sup>st</sup>-conf) factorial design. An immediate pair-repetition paradigm was used, such that within the same 1<sup>st</sup>-conf context the first face was identical across conditions (upper left corner) and only the second face varied. The row materials that were used to generate the stimuli are presented (look at **B** - the way faces were presented during the experiment). The rectangles on the template face depict the 2<sup>nd</sup>-conf; note that each colour shows a different 2<sup>nd</sup>-conf. The features were the content of these rectangles and were overlaid on the face-template based on the rectangles locations. **B.** The fMRI experiment sequence (Chapter 7.3). Note that the pair-repetition structure was "hidden". In the identity discrimination experiment, a similar sequence was used, but with an empty circle appearing before each pair, and longer ISI at the end of each pair to allow response.

Judgements that a face-pair differed depended on featural change ( $F_{1,30} = 316$ ,  $P < 0.001$ ), an effect that was more pronounced for canonical 1<sup>st</sup>-conf face-pairs (i.e. two-way-interaction features-by-orientation  $F_{1,30} = 29$ ,  $P < 0.001$ ). However note that in both 1<sup>st</sup>-conf contexts subjects' identity discrimination was significantly affected by change of features (**Fig. 7.2**).



**Figure 7.2 Identity discrimination - results**

Results are presented as a proportion of the "different" response for the eight different conditions. White bar - pairs with canonical 1<sup>st</sup>-conf, grey bar - pairs where 1<sup>st</sup>-conf is violated by inverting the inner features. Error bars are SEM. Abbreviations: Feat - features; Conf - 2<sup>nd</sup>-conf; rep - repeat; diff - different.

A change in 2<sup>nd</sup>-conf also increased subjects' tendency to judge a face-pair as having different identities ( $F_{1,30} = 24$ ,  $P < 0.001$ ) and there was a trend for this effect to be greater for canonical 1<sup>st</sup>-conf (i.e. two-way-interaction, 2<sup>nd</sup>-conf-by-orientation  $F_{1,30} = 3.4$ ,  $P = 0.07$ ). Surprisingly though, 2<sup>nd</sup>-conf affected subjects' decisions even in the context of non-canonical 1<sup>st</sup>-conf but only when features repeated ( $t_{30} = 12.1$ ,  $P < 0.001$ ), suggesting 2<sup>nd</sup>-conf information is processed even in non-canonical faces. Sensitivity to 2<sup>nd</sup>-conf change was larger when features repeated (i.e. two-way-interaction, features-by-2<sup>nd</sup>-conf:  $F_{1,30} = 7.3$ ,  $P \leq 0.01$ , **Fig. 8.2**).

1<sup>st</sup>-conf effects - Intriguingly, these results suggest that a violation of canonical 1<sup>st</sup>-conf impairs both featural and 2<sup>nd</sup>-conf processes. Thus, the data did not support the

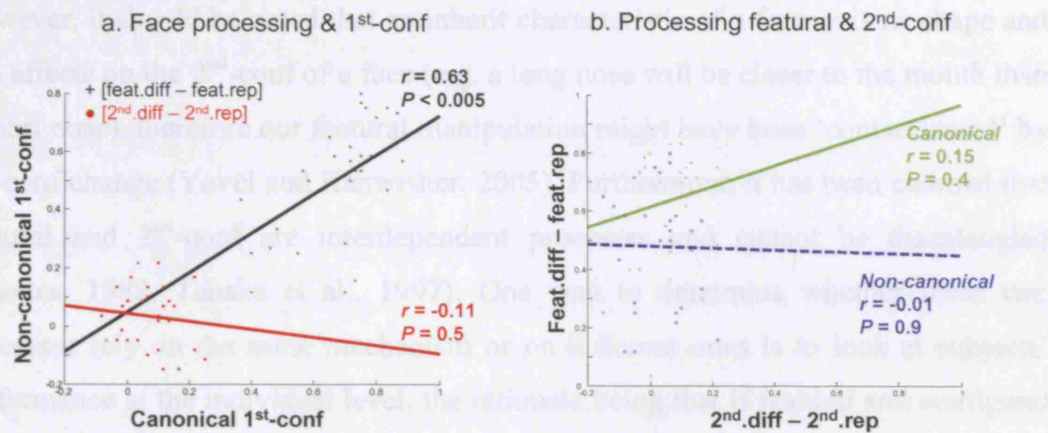
hypothesis that violation of canonical 1<sup>st</sup>-conf selectively impairs 2<sup>nd</sup>-conf processes and enhances involvement of featural processes (Diamond and Carey, 1986; Tanaka and Farah, 1993). Several recent studies showed similar results with inverted faces, challenging the configural assumption behind the face inversion effect (Sekuler et al., 2004; Gauthier et al., 1999, Yovel and Kanwisher, 2004) suggesting that an inverted face differs quantitatively but not qualitatively from an upright face (Sekuler et al., 2004). More over, in the current study an inversion mismatch face was used, as only the inner features were inverted leaving the outer contour intact and in an upright orientation, thus generating an unrealistic face (**Fig. 7.1**). Nevertheless, even with non-face stimuli as such, subjects still relied on 2<sup>nd</sup>-conf information to distinguish between these non-face stimuli (**Fig. 7.2**). To further investigate whether 1<sup>st</sup>-conf affects featural and 2<sup>nd</sup>-conf processes in the same way, I computed correlations of subjects' sensitivity to changes in both 1<sup>st</sup>-conf contexts. The rationale was that if a similar mechanism mediates featural processing in canonical and non-canonical 1<sup>st</sup>-conf faces, then performance in one 1<sup>st</sup>-conf context would predict performances in the other. A similar rationale was used for 2<sup>nd</sup>-conf processing.

Subjects' sensitivity to features was estimated using the subtraction  $\text{Feat.diff} = \text{Feat.rep}$  (averaged sensitivity for canonical:  $0.64 (\pm 0.2\text{s.d.})$ ; non-canonical:  $0.49 (\pm 0.2\text{s.d.})$ ). Similarly, sensitivity to 2<sup>nd</sup>-conf was estimated as the subtraction  $\text{2nd.diff} = \text{2nd.rep}$  (averaged sensitivity for canonical:  $0.07 (\pm 0.08\text{s.d.})$ ; non-canonical:  $0.03 (\pm 0.01\text{s.d.})$ ). As was predicted, sensitivity to featural change in canonical and non-canonical faces positively correlated (**Fig. 7.3a**;  $r = 0.685$ ,  $P < 0.001$ ). This suggests that subjects use the same mechanism for featural processing independent of 1<sup>st</sup>-conf. This finding is in accordance with previous claims that suggest that subjects' do not switch their featural processing strategy when 1<sup>st</sup>-conf changes to optimize performance (de Gelder and Rouw, 2000; Diamond and Carey, 1986). Furthermore, this finding supports the hypothesis that featural processes are not dependant on a specific 1<sup>st</sup>-conf and are therefore more likely to be used for object classification where 1<sup>st</sup>-conf is not sufficient for discrimination (Moscovitch et al., 1997). As opposed to featural processes, 2<sup>nd</sup>-conf processes were used differently depending on the 1<sup>st</sup>-conf context. Thus there was no significant correlation between sensitivity to 2<sup>nd</sup>-conf change in the canonical and non-canonical pairs (**Fig. 8.3a**;  $r = 0.16$ , n.s.).



This suggests that subjects changed their strategy depending on the 1<sup>st</sup>-conf of the face pairs (Diamond and Carey, 1986).

Taken together the results suggest that 1<sup>st</sup>-conf affected featural and 2<sup>nd</sup>-conf processing differently. Violation of canonical 1<sup>st</sup>-conf had a quantitative effect on featural processing while it had a qualitative effect on 2<sup>nd</sup>-conf processing.



**Figure 7.3 Dissociated and associated face processes**

Dissociated and associated processes were tested as correlations across subjects. Sensitivity for featural change was estimated by the subtraction: [feat.diff - feat.rep] and to 2<sup>nd</sup>-conf change: [2<sup>nd</sup>.diff - 2<sup>nd</sup>.rep], separately for each 1<sup>st</sup>-conf. **a.** scatter plots testing for process associations that depended on the 1<sup>st</sup>-conf. **b.** scatter plots testing for process association within each 1<sup>st</sup>-conf.

Feature and 2<sup>nd</sup>-confeffects – The results demonstrated that subjects are sensitive to both featural and 2<sup>nd</sup>-conf changes in a face. This finding supports the notion that both features and 2<sup>nd</sup>-conf are important cues that people rely on for individuating faces (Sergent 1984; Rhodes, 1988; Tanaka et al., 1997; Yovel and Kanwisher 2005). To compare the relative contribution of featural and 2<sup>nd</sup>-conf information in face processing I directly compared sensitivity to feature change (i.e. Feat.diff - Feat.rep) to that of 2<sup>nd</sup>-conf change (i.e. 2<sup>nd</sup>.diff - 2<sup>nd</sup>.rep). This comparison is meaningful as both these parameters were taken from real faces and hence reflect the natural variability observed outside the lab. As can be seen in **Figure 7.2** feature changes had a much larger effect on face individuation than 2<sup>nd</sup>-conf change ( $t_{30} = 16$ ,  $P < 0.001$ ). This suggests that humans rely more on features for individuating between faces than on 2<sup>nd</sup>-conf information. This is inconsistent with the configural approach to faces and the claim that subordinate discrimination (e.g. discriminating

between individual faces) is mainly based on 2<sup>nd</sup>-conf (Diamond and Carey, 1986). Support for the idea that features are sufficient to discriminate faces can be found in machine learning, where they routinely normalize a face into a standard space omitting any 2<sup>nd</sup>-conf information from it (Wiskott et al., 1997; Hancock et al., 1998, Zhang et al., 2004); therefore machines base their recognition mainly on featural information and not 2<sup>nd</sup>-conf.

However, it should be noted that an inherent characteristic of a feature is its shape and this affects on the 2<sup>nd</sup>-conf of a face (e.g. a long nose will be closer to the mouth than a short nose), therefore our featural manipulation might have been ‘contaminated’ by 2<sup>nd</sup>-conf change (Yovel and Kanwisher, 2005). Furthermore, it has been claimed that featural and 2<sup>nd</sup>-conf are interdependent processes and cannot be disentangled (Rhodes, 1988; Tanaka et al., 1997). One way to determine whether these two processes rely on the same mechanism or on different ones is to look at subjects’ performance at the individual level, the rationale being that if featural and configural processes rely on the same mechanism, then subjects’ sensitivity to feature change would predict his/her sensitivity to 2<sup>nd</sup>-conf change.

Sensitivity to featural change did not correlate with sensitivity to 2<sup>nd</sup>-conf change in either a canonical (**Fig. 7.3b**;  $r = 0.15$ , n.s.) or non-canonical contexts ( $r = 0.1$ , n.s.). This analysis supports the idea that featural and 2<sup>nd</sup>-conf information from a face are processes that to some extent use separate mechanisms. This result is in accordance with findings from principle component analysis (PCA) of face perception, where two separate components were identified: a featural (termed ‘texture’) and a 2<sup>nd</sup>-conf (termed ‘shape’; Hancock et al., 1996).

To further test the dissociation between featural and 2<sup>nd</sup>-conf processing, I conducted an fMRI experiment. The assumption here was that if featural and 2<sup>nd</sup>-conf processes are dissociable, as the behaviour results suggest they would also be represented in different brain regions.



## 7.3 PAIR REPETITION PARADIGM – AN fMRI STUDY

### 7.3.1 *Methods*

**Subjects.** 14 healthy volunteers participated (9 females, mean age 29y, range 19-51y, 12 right handed) in the fMRI experiment. All had normal vision and no concurrent or past neurological or psychiatric history. Informed consent was obtained according to procedures approved by the Joint Ethics Committee of the National Hospital for Neurology and Neurosurgery (NHNN) and Institute of Neurology (ION), London.

**Stimuli.** Identical stimuli were used as in the identity discrimination experiment.

**Experimental procedure.** An immediate pair repetition paradigm was used (Courtzi and Kanwisher, 2000; see **Chapter 5**). The factorial design was identical to the one used in the identity discrimination experiment with three factors: 2 (features repetition) by 2 (2<sup>nd</sup>-conf repetition) by 2 (1<sup>st</sup>-conf context). The experiment included 15 pairs for each of the 8 conditions; each pair was presented three times in three different consecutive fMRI sessions. The order of trials was pseudo random to maximize separation in time between repeating of faces with the same features or 2<sup>nd</sup>-conf. A further ~30% of the total trials were null events in which only a fixation point was presented. Faces were presented for 500ms with an inter-stimuli-interval of 1500ms in which a fixation point appeared (**Fig. 7.1b**). Subjects were instructed to maintain fixation and to indicate for each face whether the inner features were upright or inverted, using the right middle and index fingers (counterbalance across subjects). Note that the task was unrelated to the repetition manipulation and faces appeared in a continuous stream; hence the pair-repetition structure of the experiment was hidden. Each fMRI session was divided into two epochs with a 5s break in which the subjects received feedback on their performances (i.e. percent correct responses and reaction time). The feedback was given overall performances independent of conditions and served as a motivational cue. 13 subjects performed the identity discrimination experiment immediately after the fMRI session (see above).

**Scanning.** A Siemens 1.5T Sonata system (Siemens, Erlangen, Germany) was used to acquire 32 oblique axial slices (2 mm thick with 1.5mm gap) with 64\*64 pixels

and in-plane resolution of  $3 \times 3 \text{ mm}^2$ ,  $90^\circ$  flip-angle, 30ms echo time (TE) and 2880s repeat time (TR).

**Data analysis.** Whole-brain voxel-based analyses were performed using SPM2 ([www.fil.ion.ucl.ac.uk/spm](http://www.fil.ion.ucl.ac.uk/spm)). EPI volumes were spatially realigned, unwrapped, temporally realigned, normalized and smoothed.

In the first level, the design matrix had eight regressors with the onset of the second event of each pair type. Effects of no interest included regressors for feedback events, and scanning session effects. Linear contrasts pertaining to the main effects, interactions and simple effects were calculated for each subject. To allow inferences at the population level, a second-level analysis was performed, in which images resulting from contrasts for each subject were entered into a new model (i.e. one-sample t-test), which treated subjects as a random effect. Correlations with inter-subject variability in perceived differences between pairs (see below) were tested by using a simple correlation analysis across subjects between the relevant behavioural measurements and the contrast images (i.e. for featural change:  $\text{Feat.diff} - \text{Feat.rep}$ ; for 2<sup>nd</sup>-conf change:  $2^{\text{nd-conf.diff}} - 2^{\text{nd-conf.rep}}$ ).

As mentioned before the focus of this thesis is in dissociating processes within occipito-temporal cortices (see **Chapter 1**). Therefore I concentrated on activations from these regions, but for completeness reported in the tables all regions showing significant effects above the threshold of  $P < 0.001$  uncorrected.

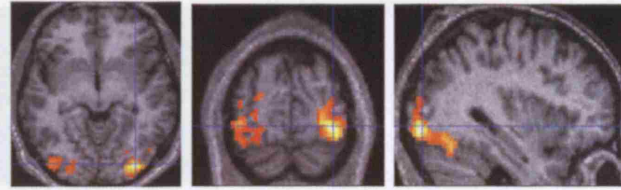
### **7.3.2 Results & Discussion**

Sensitivity to violations of 1<sup>st</sup>-conf was tested by comparing the responses of canonical and non-canonical pairs. An increased response for non-canonical pairs compared to canonical was observed along the bilateral posterior occipital cortex with maxima in the IOG but with an extended activation that encompassed posterior FFG (see **Fig. 7.4** and **Table 7.1a**). No above threshold activation was observed for larger response for canonical compared to non-canonical pairs.

**Figure 7.4: Violation of 1<sup>st</sup>-conf**

Increased activation following violation compared to canonical 1<sup>st</sup>-conf overlaid on single subject canonical T1 image.

Main effect of 1<sup>st</sup>-conf (violation > canonical)



$P < 0.001$

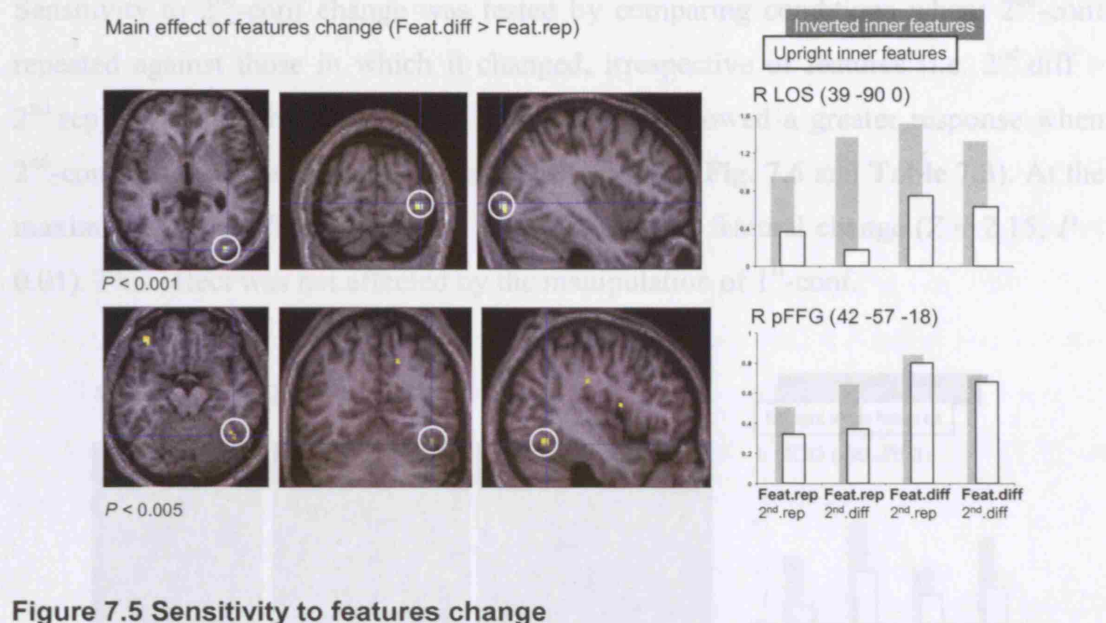
**Table 7.1**

Main effect of 1<sup>st</sup>-conf:  
*violated > canonical*

Anatomical location	H	Z-stat	MNI(x,y,z)
LingG L	3.92	-9 -84 -15	
IOG R	5.21	36 -87 -6	
L	3.62	-42 -75 -12	
pFFG R	4.19	39 -63 -24	
	4.18	39 -69 -15	
LOS L	3.90	-39 -87 -3	
MOG R	3.85	21 -105 9	
CG	3.97	0 -18 42	

Abbreviations: LingG, Lingual gyrus; IOG, inferior occipital gyrus; pFFG, posterior fusiform gyrus; LOS, lateral occipital sulcus; MOG, middle occipital gyrus; CG, cingulate gyrus; H, hemisphere; L, left; R, right.

Sensitivity to feature changes was tested by comparing conditions where features repeated against conditions where they changed independently of the 2<sup>nd</sup>-conf manipulation (i.e.  $\text{Feat.diff} > \text{Feat.rep}$ ). The right lateral occipital sulcus (LOS), left inferior occipital gyrus (IOG) and right fusiform gyrus (FFG, **Fig. 7.5** and **Table 7.2**) showed less activation when features were repeated compared to when they changed. To test for a specific sensitivity of this region to featural change but not to 2<sup>nd</sup>-conf a further analysis was performed directly by comparing the effect of featural against 2<sup>nd</sup>-conf changes. Only the right LOS showed greater sensitivity to featural change over 2<sup>nd</sup>-conf change ( $Z = 2.77$ ;  $P < 0.005$ ). In addition, the effect of featural change in these regions was not influenced by the 1<sup>st</sup>-conf manipulation (see **Table 7.2b**). An interaction between 1<sup>st</sup>-conf and feature change was observed in anterior medial temporal regions, where sensitivity to feature changes was stronger for canonical 1<sup>st</sup>-conf faces.



**Figure 7.5 Sensitivity to features change**

On the left SPMs maps showing stronger response to pairs where featured changed compare to ones where it was repeated overlaid on the single subject canonical T1 image. On the right the parameter estimates for each of the eight conditions taken from the maxima circled in white.

**Table 7.2**

Anatomical location	H	Z-stat	MNI(x,y,z)
---------------------	---	--------	------------

**a. Main effect Feature repetition:**

*Feat.diff > Feat.rep*

LOS R	3.61	39 -90 0
IOG L	2.94	-48 -78 -15
pFFG R	2.7	45 -57 -18
OFC L	3.18	-39 42 -18
Insula L	3.14	-33 -9 6

**b. Interaction 1<sup>st</sup>-conf-by-Feature:**

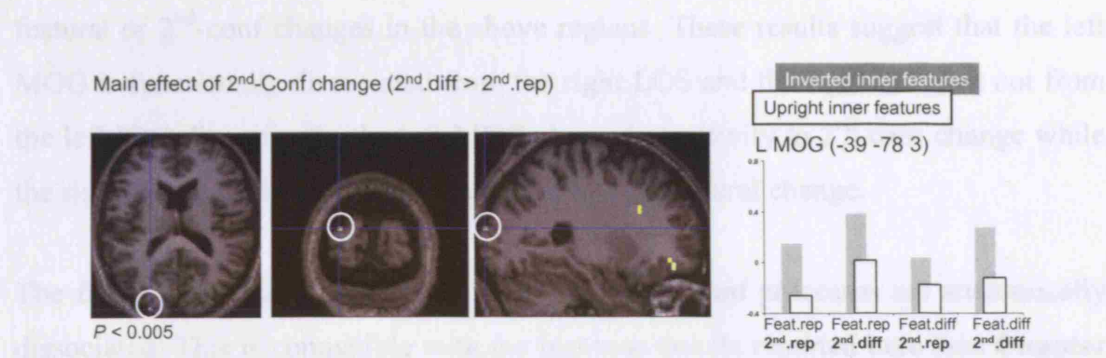
*canonical: Feat.diff > Feat.rep & non-canonical: Feat.rep < Feat.diff*

ITG R	3.08	42 3 -42
L	3.73	-36 -18 -33
aHipp L	3.70	-30 -9 -27
Amyg L	3.67	-30 0 -21
aSTS L	3.45	-42 9 -30
CG M	4.06	-3 39 12
aCal L	3.86	-12 -48 9

Abbreviations: LOS, lateral occipital sulcus; IOG, inferior occipital gyrus; pFFG, posterior fusiform gyrus; OFC, orbital frontal cortex; ITG, inferior temporal gyrus; aHipp, anterior hippocampus; Amyg, amygdala; aSTS, anterior superior temporal sulcus; aCal, anterior calcarine sulcus.



Sensitivity to 2<sup>nd</sup>-conf change was tested by comparing conditions where 2<sup>nd</sup>-conf repeated against those in which it changed, irrespective of features (i.e. 2<sup>nd</sup>.diff > 2<sup>nd</sup>.rep). The left middle occipital gyrus (MOG) showed a greater response when 2<sup>nd</sup>-conf changed compared to when it was repeated (**Fig. 7.6** and **Table 7.3**). At the maxima the latter effect was larger than the effect of featural change ( $Z = 2.15$ ;  $P < 0.01$ ). This effect was not affected by the manipulation of 1<sup>st</sup>-conf.



**Figure 7.6: Sensitivity to 2<sup>nd</sup>-conf change**

On the left SPMs maps showing a stronger response to pairs where 2<sup>nd</sup>-conf changed compared to ones where it was repeated overlaid on the single subject canonical T1 image. On the right, the parameter estimates for each of the eight conditions taken from the maxima, circled in white.

**Table 7.3**

Anatomical location	H	Z	MNI(x,y,z)
---------------------	---	---	------------

**Main effect 2nd-Conf repetition:**  
2<sup>nd</sup>.diff > 2<sup>nd</sup>.rep

MOG L	2.63	-39 -78 3	
Cerebellum	M	4.29	0 -51 -48
Cuneus	R	3.10	18 -78 21

Abbreviations: MOG, middle occipital gyrus; L, left, M, middle, R, right

Taken together, these findings suggest a functional dissociation between different regions within posterior occipital cortices. To test this formally, an ANOVA with four factors was computed: regions (left MOG, right LOS), featural changes (Feat.diff, Feat.rep), 2<sup>nd</sup>-conf changes (2<sup>nd</sup>.Diff, 2<sup>nd</sup>.Rep) and 1<sup>st</sup>-conf (canonical,

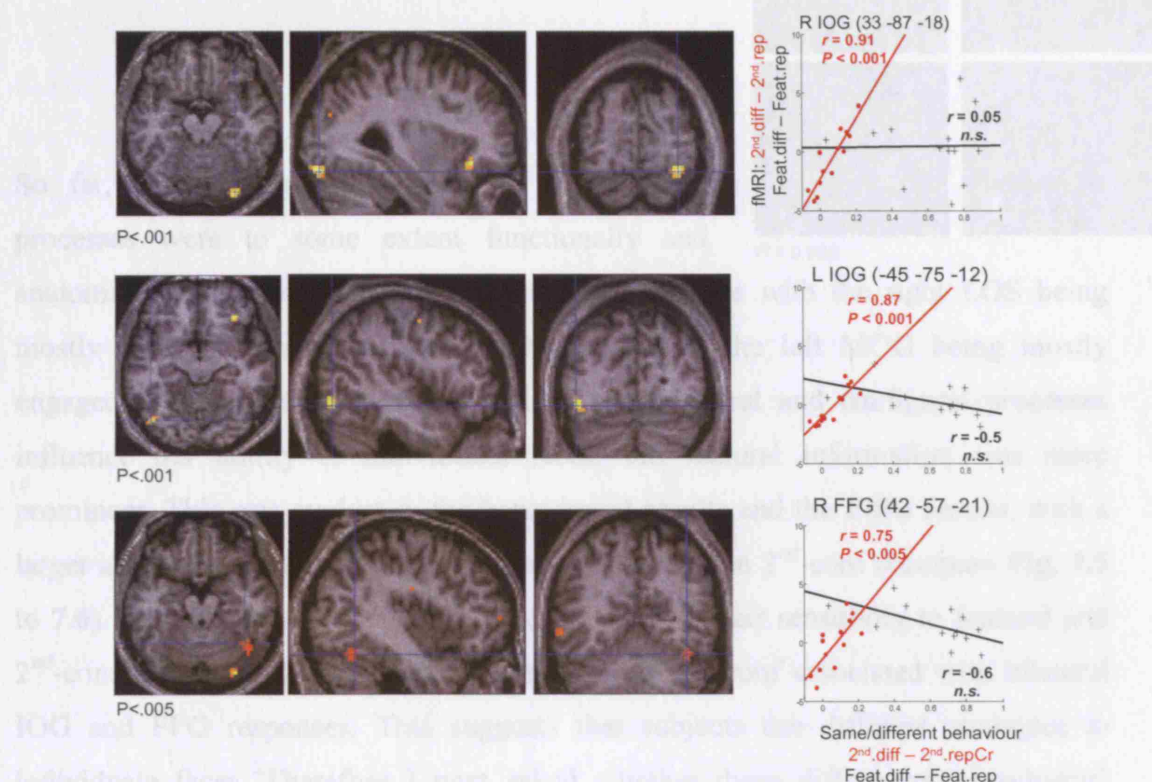
violated). This confirmed an interaction of regions by feature change ( $F_{1,13} = 20, P \leq 0.001$ ), and a region by 2<sup>nd</sup>-conf changes ( $F_{1,13} = 6.8, P < 0.05$ ). Functional dissociation between the left MOG and right FFG was also confirmed by an interaction of region by feature changes ( $F_{1,13} = 10, P < 0.005$ ), and region by 2<sup>nd</sup>-conf change ( $F_{1,13} = 6.6, P < 0.05$ ). The left MOG response did not significantly differ from left IOG. Face-pair orientation did not significantly interact with either featural or 2<sup>nd</sup>-conf changes in the above regions. These results suggest that the left MOG is functionally dissociated from the right LOS and the right FFG but not from the left IOG. Specifically the left MOG showed sensitivity to 2<sup>nd</sup>-conf change while the right LOS and right FFG showed sensitivity to featural change.

The fMRI results so far show that featural and 2<sup>nd</sup>-conf processes are anatomically dissociated. This is compatible with the previous results reported here (see **Chapter 6**) that suggest that posterior occipital regions decompose a face to its basic components (Lerner et al., 2001; Farah et al., 1998). Occipital cortices, in discordance with the behaviour study reported above, did not show reliable evidence for an interaction between 2<sup>nd</sup>-conf and featural processes. This might suggest that these interactions arise from involvement of other regions (such as anterior medial temporal cortices).

Next I tested whether subjects' perceived sensitivity to feature and 2<sup>nd</sup>-conf changes affect their brain responses. This hypothesis was tested by correlating subjects' ( $n = 13$ ) sensitivity to feature and 2<sup>nd</sup>-conf changes measured in the identity discrimination experiment with that measured in the fMRI experiment, separately for canonical and non-canonical 1<sup>st</sup>-conf. No correlations were observed for sensitivity to featural change. This lack of correlation might be due to a ceiling effect in sensitivity to features; as mentioned before subjects were highly sensitive to change in features.

Perceived sensitivity to 2<sup>nd</sup>-conf changes positively correlated with the size of 2<sup>nd</sup>-conf change effect in bilateral inferior occipital gyrus and in the right FFG (**Fig. 7.7** and **Table 7.4**). In these regions, subjects that showed greater perceived sensitivity to 2<sup>nd</sup>-conf change (measured in the identity discrimination experiment) also showed a larger change in the BOLD response for a change in the 2<sup>nd</sup>-conf information.

Perceptual sensitivity to feature changes did not correlate with brain sensitivity to these changes. Note that the left IOG and right FFG showed sensitivity to both 2<sup>nd</sup>-conf (that was dependent on subjects' perception) and sensitive featural change. Response to featural changes in right IOG and to 2<sup>nd</sup>-conf in the right LOS did not overlap (see Fig. 7.8).



**Figure 7.7: Correlation behaviour and fMRI**

On the left SPMs maps showing positive correlation of sensitivity to 2<sup>nd</sup>-conf changes overlaid on the single subject canonical T1 image. On the right scatter plots of the correlations where fMRI values of the effect size taken from the maxima correlated with subjects' sensitivity measured behaviourally, separately for 2<sup>nd</sup>-conf and feature change.

**Table 7.4: correlation behaviour and fMRI**

2<sup>nd</sup>-Conf sensitivity, 2<sup>nd</sup>.diff – 2<sup>nd</sup>.rep

Anatomical location	H	Z	MNI(x,y,z)
IOG	R	4.31	33 -87 -18
	L	3.85	-51 -75 -12
pFFG	R	2.93	42 -57 -21
IFG	L	4.54	-33 36 24
SFG	R	4.11	18 63 12
		4.06	18 3 54
CG	M	4.06	-6 -9 36
IFG/insula	R	3.75	33 33 -12
Putamen	L	3.50	-27 0 9

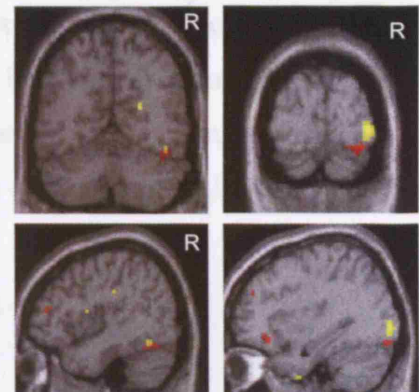
Abbreviations: H: Hemisphere; R: Right; L: Left; IOG: inferior occipital gyrus; FFG: posterior occipital gyrus; MOG: middle occipital gyrus; CG: cingulate gyrus; LingG: lingual gyrus; LOS: lateral occipital sulcus; OFC: orbital frontal cortex; ITG: inferior temporal gyrus; aHipp: anterior hippocampus; Amyg: amygdala; aSTS: anterior superior temporal sulcus; aCal: anterior calcarine. Minimum  $t_{26} = 2.34$ .



**Figure 7.8: Overview fMRI effects.**

SPMs overlaid on the single subject canonical T1 image. On the right coronal and sagittal views of the right FFG response to both feature and 2<sup>nd</sup>-conf changes that was dependent on subjects' perceived sensitivity. On the left coronal and sagittal views of right LOS and IOG that responded differently to featural and 2<sup>nd</sup>-conf change.

Feat.diff – feat.rep

2<sup>nd</sup>-Conf correlation same-diff & fMRI $P < 0.005$ 

So far, I have shown that featural and 2<sup>nd</sup>-conf processes were to some extent functionally and anatomically dissociated in posterior occipital cortices with the right LOS being mostly engaged mostly in featural processing and the left MOG being mostly engaged mostly in configural processing. Both featural and configural processes influence our ability to individuate faces, but featural information was more prominent. This was evident in the behavioural results and the fMRI results, with a larger and more robust repetition effects for feature than 2<sup>nd</sup>-conf (compare **Fig. 7.5** to **7.6**). The results also suggest that people vary in their sensitivity to featural and 2<sup>nd</sup>-conf change, with the extent of sensitivity to 2<sup>nd</sup>-conf associated with bilateral IOG and FFG responses. This suggests that subjects use different strategies to individuate faces. Therefore I next asked whether these differences in subjects' strategies to individuate faces have any ecological value, and specifically whether they affect face recognition.

## 7.4 THE ROLE OF FEATURAL AND 2<sup>ND</sup>-CONF INFORMATION IN FACE RECOGNITION

As discussed above (see **7.1, Introduction**), the configural approach to face processing predicts that 2<sup>nd</sup>-conf and not features are the crucial in allowing face recognition. Recall, for example, that neuropsychological research demonstrates that congenital prosopagnosic subjects show impairment in perceiving 2<sup>nd</sup>-conf information from a face but not in the perception of facial features (Barton et al.,



2003). The aim of the following studies was to test whether variability in face perception observed in healthy subjects, specifically in their sensitivity to featural and 2<sup>nd</sup>-conf changes, predicts their face recognition skills. Three measurements of face recognition skill were used: a subjective rating and two objective measures. The objective measures were two face recognition tests, one based on incidental learning of unfamiliar faces and a second was a familiarity judgement task of famous faces. I first describe each measurement in more detail and then present the results of all the three together.

### ***7.4.1 Methods***

**Subjects.** 19 healthy volunteers participated (9 females, mean age 25y, range 18-35y). All had normal vision and no concurrent or past neurological or psychiatric history. One subject failed to use the correct response buttons and was excluded from analysis.

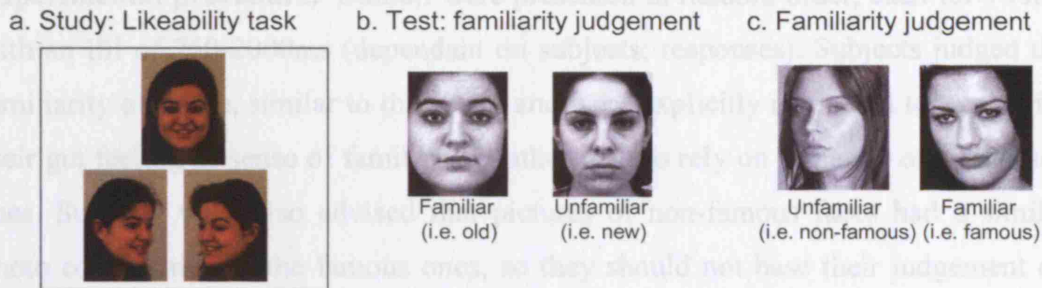
#### ***Estimation of subjects' face recognition skill***

Subjective measure – self rating: Subjects were requested to rate their face recognition skill on a scale of 1-to-10. Ten being 'I never forget a person's face once I have met him' and one being 'I cannot remember faces at all'. Subjects were explicitly instructed that their self rating should be dissociated from their naming skills and their ability to retrieve any semantic information regarding individuals, but it should reflect their sense of familiarity. The subjective measure was also obtained from subjects who participated in the fMRI experiment (see above, n=13) and from the current cohort of subjects (n=18). The difference in procedure between the two cohorts of subjects related to the time when the question was introduced, the first cohort of subjects were asked to rate themselves at the end of the experimental session (i.e. after the fMRI & the identity discrimination experiments); the second cohort of subjects were asked to rate themselves at the beginning of the experimental session.

Objective measure 1 - Incidental recognition test of unfamiliar faces:

**Stimuli.** 40 identities (20 females) were taken from the Karolinska Directed Emotional Faces set (KDEF, Lundqvist, et al., 1998). These were different identities to the one used in the identity discrimination and fMRI experiments (see above). In the *study phase* coloured close-ups (shoulder level) of happy facial expressions were simultaneously presented in three different view points (front, left  $\frac{3}{4}$ , right  $\frac{3}{4}$  views) (**Fig. 7.9a**). In the *test phase*, images of the same identity were used, though this time they were achromatically presented in extreme close-ups of the frontal view and the expressions were neutral (**Fig. 7.9b**).

**Experimental procedure.** In the incidental *study phase*, a likeability rating judgement task was used. Subjects were presented with three different views of the same individual with a happy expression for 5s (**Fig. 8.9a**). After the faces disappeared from the screen they were prompted with a question asking them to state how much they liked this person on a scale from 1-to-6; with 1 being 'I don't like this person at all' and 6 being 'I like this person very much and would be happy to meet him/her'). The next identity appeared after subjects gave their rating. 20 identities (10 females) from a total of 40 were chosen randomly for the *study phase*. An incidental learning and likeability task was used in order to accurately simulate real life experiences. Subjects were exposed to more than 300 other faces between the *study* and the *test phase*. These other faces were presented as part of 3 different experiments involving faces. The experiments were the familiarity judgement of famous faces (see below), identity discrimination task (see above), and a similarity task of morphed famous faces (reported in **Chapter 4**). The average duration between study and test was ~45min. In the *test phase*, subjects performed a familiarity judgement ("Does the face look familiar to you?") on 40 identities, of which 20 were presented in the *study phase*. Subjects were explicitly instructed that these faces were of people that might have appeared previously in one of the preceding experiments, and if they had, a different image of that person would have been used. More so, they were instructed to work with their gut feeling of a sense of familiarity, rather than rely on contextual cues. Faces were presented in random order, each for 750ms, with an ISI of 1000-2000ms (dependant on subjects' reaction time).



**Figure 7.9: Experimental design: Objective measure of face recognition skills**

Two objective measures were used to estimate subjects' face recognition skill. Incidental learning task of unfamiliar faces, **a**. Example of stimuli presented in the study phase on which subjects performed a likeability test. **b**. Example of stimuli used in the test phase, on which subjects performed familiarity judgements. Note that different images were used in the study and test phases (e.g. different expression, different colours, different view condition): this was done to minimize possible confounds of pictorial cues that are not related to facial identities. **c**. familiarity judgement of famous and non-famous faces. Note that an effort was made in the choice of the non-famous faces to match the pictorial composition of the photos to that of the famous faces.

**Data analysis.** Data were analyzed using signal detection theory. For each subject sensitivity signal to 'familiarity' (i.e.  $d'$ ) and the decision criterion (i.e.  $\beta$ ; subjects' bias) were estimated (Snodgrass and Colwin, 1988). Correct recognition of a previously seen face was defined as a *hit*, while a feeling of familiarity arising from a new face was defined as a *false alarm*.  $d'$  sensitivity was estimated as the difference between the Z scores of the hit rates (H) and of the false alarm rates (FA)

$$d' = - Z_H - Z_{FA}$$

Decision criteria ( $\beta$ ) was estimated as the ratio of the densities of the hit and false alarm rates. It was calculated as

$$\beta = f_0(Z_H) / f_n(Z_{FA})$$

where  $f_0$  is the height of the normal distribution over  $Z_H$  and  $f_n$  is the height of the normal distribution over  $Z_{FA}$  (Snodgrass and Colwin, 1988).

#### Objective measure 2 - Familiarity judgement of famous faces:

**Stimuli.** 114 achromatic close-ups of famous people and 114 achromatic close-ups of non-famous faces were used (**Figure 8.9c**). An effort was made to match the photo composition of the non-famous faces to these of the famous faces, by using for example photos taken from unknown models' books, and of local politicians in distant regions. A pilot study confirmed the anonymity of the unknown faces.

**Experimental procedure.** Stimuli were presented in random order, each for 750ms with an ISI of 750-2000ms (dependant on subjects; responses). Subjects judged the familiarity of a face, similar to the above and were explicitly instructed to work with their gut feeling of sense of familiarity, rather than to rely on semantic or contextual cues. Subjects were also advised that pictures of non-famous faces had a similar photo composition to the famous ones, so they should not base their judgement on photo composition.

**Data analysis.** Data were analyzed using signal detection theory, in an identical procedure as the incidental learning task described above.

**The correlation matrix (Table 7.5)** was calculated using non parametric spearman correlations SPSS11.0, with each subject having one score in each behavioural measure. Significance was estimated with a one-tailed distribution as any increase in sensitivity was expected to positively correlate with estimation of face recognition skill. In the recognition test of unfamiliar faces, two subjects did not make ‘false alarms’, hence preventing a reliable estimation of their decision criterion ( $\beta$ ), therefore correlations with that factor are based on 16 subjects.

#### ***8.4.2 Results & Discussion***

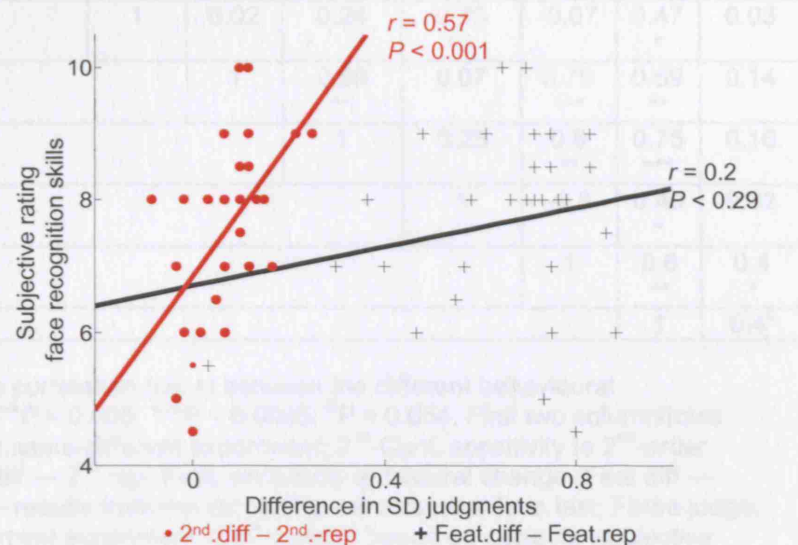
Intriguingly, subjects’  $d'$  and  $\beta$  were highly correlated across the two objective measures of face recognition: the unfamiliar and famous face recognition tests (**Table 7.5**). These correlations suggest that subjects rely on the same cognitive mechanism to extract a familiarity signal of unfamiliar (newly learned) and well known familiar faces. This is inconsistent with Bruce and Young’s (1986) original proposition (see **Chapter 1**) that dissociates recognition of familiar from unfamiliar faces.

Surprisingly, the subjective rating of self recognition skill did not correlate with any of the two objective measures of  $d'$  sensitivity to ‘familiarity’ signal. Self rating correlated positively with the decision criteria in the famous face recognition task; this might have been expected as subjects rated themselves prior to the experiment and therefore their responses may have been biased (**Table 7.5**).

More interestingly, the subjective measure of face recognition skill positively correlated with subjects' sensitivity to 2<sup>nd</sup>-conf in the context of canonical 1<sup>st</sup>-conf. No correlation with face recognition skill and sensitivity to feature change was observed (**Fig. 7.10**), in either of the 1<sup>st</sup>-conf contexts.

**Figure 7.10:**  
correlation with  
subjective rating of  
face recognition skill

The subjective face recognition skill Y-axis plotted against the sensitivity to feature change black '+' and 2<sup>nd</sup>-conf red '•' X-axis. The scatter plots responses collapsed across the two cohorts of subjects ( $n=31$ ; see **7.4.1 Methods**).



This result was observed in two different cohorts of subjects with a slightly different procedure (see **7.4.1 Methods**). In the first cohort, subjects performed the identity discrimination experiment first and were then asked to estimate their face recognition skill ( $n = 13$ , correlation of recognition skills with sensitivity to 2<sup>nd</sup>-conf. change - canonical:  $r = 0.75$ ,  $P < 0.001$ ; non-canonical:  $r = -0.27$ ,  $P = 0.19$ ; features - canonical:  $r = 0.24$ ,  $P = 0.46$ ; non-canonical:  $r = -0.17$ ,  $P = 0.22$ ). In the second cohort, subjects were asked to estimate their face recognition skill before performing the experiment, and the results were replicated ( $n = 18$ , 2<sup>nd</sup>-conf. canonical:  $r = 0.54$ ,  $P < 0.01$ ; non-canonical:  $r = -0.3$ ,  $P = 0.1$ ; features canonical:  $r = 0.12$ ,  $P = 0.3$ ; non-canonical:  $r = -0.03$ ,  $P = 0.4$ , **Table 7.5**).



**Table 8.5: Correlation matrix of behaviour experiments:**

		Identity discrimination		Recog. Unfam.			Fame judge.			Self rating
		2 <sup>nd</sup> -Conf	Feat.	d'	$\beta$	hit	d'	$\beta$	hit	
Iden. discr.	2 <sup>nd</sup> -Conf	1	0.23	<b>0.45</b> *	0.06	-0.03	<b>0.43</b> *	0.1	0.46 *	<b>0.55</b> **
	Feat.		1	0.2	-0.03	0.24	<b>0.44</b> *	-0.15	0.25	0.12
Recog Unfam	d'			1	0.02	0.24	<b>0.79</b> ***	-0.07	0.47 *	0.03
	$\beta$				1	0.59 **	0.07	<b>0.79</b> ***	0.59 **	0.14
	Hit					1	0.25	0.6 **	0.75 ***	0.16
Fame judge	d'						1	-0.3	0.48 *	0.02
	$\beta$							1	0.6 **	0.4 *
	Hit								1	0.4 <sup>£</sup>

The numbers represent the correlation (i.e.  $r$ ) between the different behavioural measurements. \* $P < 0.05$ ; \*\* $P < 0.005$ ; \*\*\* $P < 0.0005$ ; <sup>£</sup> $P = 0.054$ . First two column/rows refer to the results from the same-different experiment; 2<sup>nd</sup>-Conf, sensitivity to 2<sup>nd</sup>-order configuration change (2<sup>nd</sup>.diff — 2<sup>nd</sup>.rep) Feat, sensitivity to featural change (Feat.diff — Feat.rep); Recog. Unfam. — results from the recognition of unfamiliar face test; Fame judge. — results of the fame judgement experiment. Self rating is based on subjects' subjective rating of their face recognition skill.

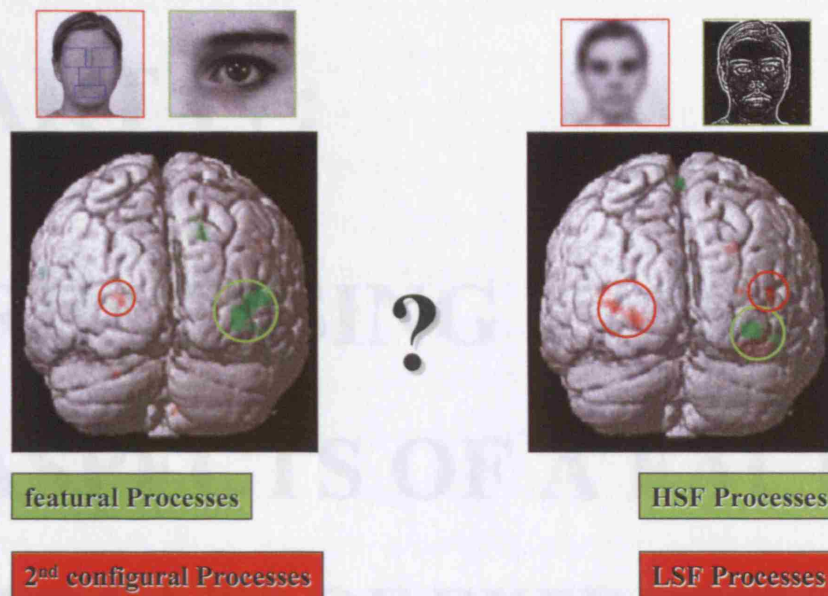
The ability to predict subjects face recognition skill based on her/his sensitivity to 2<sup>nd</sup>-conf. change in canonical faces was confirmed by the two objective measurements (**Table 7.5**). Sensitivity to 2<sup>nd</sup>-conf positively correlated with the ability to correctly detect familiar faces (i.e.  $d'$ ) in the unfamiliar incidental recognition test ( $r = 0.45$ ;  $P < 0.05$ ), and in the familiarity judgement of famous faces ( $r = 0.44$ ;  $P < 0.05$ ), but only in the context of canonical 1<sup>st</sup>-conf. Sensitivity to featural change in canonical 1<sup>st</sup>-conf positively correlated with  $d'$  of famous faces but not with that of unfamiliar faces (**Table 7.5**).

These results demonstrate that subjects who were more sensitive to 2<sup>nd</sup>-conf change while discriminating between faces had better face recognition skills. This finding is compatible with reports of prosopagnosic patients, especially congenital ones who show impairment in 2<sup>nd</sup>-conf processing (de Gelder and Rouw, 2000; Barton et al., 2003). Based on the findings here, one intriguing option is that congenital prosopagnosic patients are quantitatively rather than a qualitatively different from the normal healthy population. In fact they might perform within the normal

distribution of face recognition skills of the healthy population. An intriguing question is whether training one to detect and encode 2<sup>nd</sup>-conf will improve her/his face recognition skills as well, as suggested by this result. The result demonstrated that sensitivity to featural change also predicted subjects'  $d'$  sensitivity to recognition of famous faces. This suggests that in the cases of extensive prior experience, sensitivity to featural information in a face might be sufficient to establish recognition.

## 7.5 SUMMARY

The two studies described here (**Chapter 6, 7**) provide evidence for dissociable processes of face information in posterior occipital cortices. They suggest that early face processes decompose a face image to different components that later converge in more anterior regions along the ventral visual pathways, namely the FFG with the left MOG processing configural and LSF information while the right LOS processes featural information and right IOG processes HSF information. In some subjects bilateral IOG was additionally recruited in the processing of 2<sup>nd</sup>-conf of canonical faces: this additional processing improved subjects' face recognition.



**Figure 7.11: Early face processes in posterior occipital cortices.**

On the left, regions within posterior occipital that showed differential sensitivity to features or 2<sup>nd</sup>-conf change overlaid on rendered brain. On the right, regions within posterior occipital that showed differential sensitivity to HSF or LSF change overlaid on a rendered brain.

There was an intriguing similarity between the results of the two fMRI experiments (**Fig. 7.11**). Regions within left MOG showed sensitivity to LSF and 2<sup>nd</sup>-conf information in a face while regions within right lateral occipital cortex showed sensitivity to HSF (right IOG) and featural information (right LOS). This similarity might suggest some support to the hypothesis that relates featural processing to HSF information, and configural processing to LSF information (Farah et al., 1998). On the other hand, the right IOG was involved in HSF and 2<sup>nd</sup>-conf processing that was dependent on subjects' perception. This might suggest that this hypothesis is too simplified and further research should be done to clarify it.

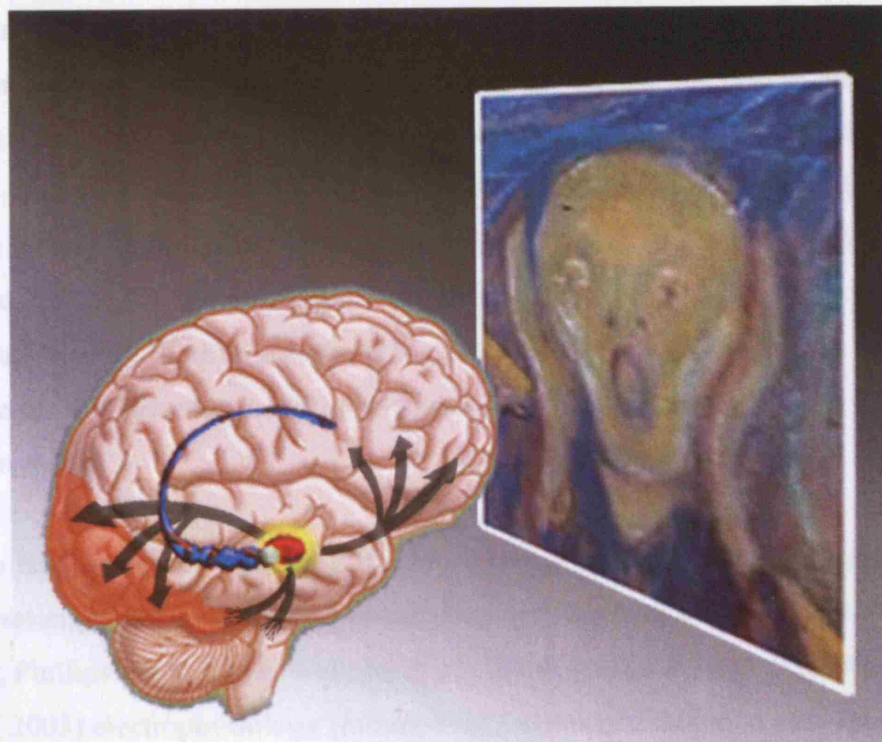


# **PART IV:**

## **PROCESSING VARIANT**

### **ASPECTS OF A FACE:**

### **THE CASE OF EXPRESSIONS**



So far I have focused on two aspects of faces: physical properties and identity. Physical properties of a face vary depending on viewing conditions, expression, age, makeup etc. Identity, on the other hand is an invariant property of a face, as it is independent of viewing conditions and of any other variant properties of a face (Haxby et al., 2000). Several face processing models suggest that following an initial physical processing of a face, variant aspects such as expression are further processed using a separate pathway from those used for identity (Bruce and Young, 1986; Haxby et al., 2001, see **1.1 Introduction** for review). Others argue that facial expression processing diverges even earlier, prior to processing of physical properties. This route is suggested to circumvent initial visual processing of a face (i.e. occipital cortex) via a superior colliculus – pulvinar - amygdala pathway (Morris et al., 1998; Vuilleumier et al., 2001, 2003, 2004; Pegna et al., 2005). It has been suggested that this pathway is involved when a face communicates salient information, such as a threat cue (e.g. fearful expression; Morris et al., 1998; Vuilleumier et al., 2001, 2003, 2004; de Gelder et al., 2004, Das et al., 2005; Liddel et al., 2005). Some ERP studies demonstrate an early (135ms post stimuli) expression effect that precedes the face specific wave N170, supporting a fast route hypothesis for processing expressions (Eimer and Holmes, 2002, Streit et al., 2003). This effect has been localised to the left amygdala (Streit et al., 2003) though these findings have not been replicated by others (Sato et al., 2001; Esslen et al., 2004; Holmes and Eimer, 2003; Batty and Taylor, 2003). Indeed, not all researchers support the idea of a fast collicular-pulvinar-amygdala expression route (Krolak-Salmon et al., 2004; Pessoa et al., 2003). One aim, here, was to test the fast route expression processing hypothesis, focusing on the role of the amygdala.

There is a consensus regarding the involvement of the amygdala in processing expression, as demonstrated by neuroimaging (Morris et al., 1996; Brieter et al., 1996; Phillips et al., 2004; Winston et al., 2004; Vuilleumier et al., 2001; Pessoa et al., 2003) electrophysiology (Intracranial recording: Fried et al., Krolak-Salmon et al., 2004; Scalp recording: Streit et al., 2003) and by some lesion studies (e.g. Adolphs et al., 1999; Young et al., 1995; Calder et al., 1996; Broks et al., 1998;

Calder et al., 2001). Non-confirmatory lesion studies have also been reported (Hamann and Adolphs, 1999; Rapsak et al., 2000).

The inconclusive results from lesion studies suggest that the exact role of the amygdala in processing expression remains unclear, specifically regarding explicit perception of expression. One possible reason for this relates to the unspecific and variable aetiology, and extent of lesions tested and compared. Most studies examined extensive lesions to anterior temporal pole that included damage to the amygdala, hippocampus, anterior temporal poles and other adjoining structures. These lesions typically arise following temporal lobectomy (Anderson et al., 2000; Adolphs et al., 2001; Brierley et al., 2005) or encephalitis (Broks et al., 1998; Adolphs et al., 2003). A few studies have tested medial temporal sclerosis (MTS) epileptic patients with lesions involving the hippocampus that in some cases extend to the amygdala (Meletti et al., 2003; Benuzzi et al., 2004). Studies of patients with a restricted lesion to the bilateral amygdala involve patients with the genetic syndrome known as the Urbach-Wiethe syndrome (Adolphs et al., 1994, 1995; Siebert et al., 2003). Thus, only a few studies have compared patients group with similar aetiology and relatively restricted and well defined lesions. Therefore a second aim here was to compare expression perception and brain responses of two temporal epileptic patient populations with and without lesions to the amygdala, in order to establish the effect of the abnormal amygdala on expression perception and brain response.

Two previous fMRI studies tested the effect of temporal epilepsy on processing fearful expressions. Benuzzi et al. (2004) report that patients with right epileptic focus show impaired fearful perception and correspondingly had less activation in occipito-temporal and inferior frontal regions compared to patients with left epileptic focus and controls. Vuilleumier et al. (2004) restricted patients they examined to those with well-defined left temporal lobe epilepsy. They report that lesions that included the amygdala attenuate a fear-induced enhancement of activity in occipito-temporal and frontal regions. Here, I adopt a similar strategy to Vuilleumier et al. (2004) in a patient study (**Chapter 9**) to replicate their findings and expand on these observations by including a temporal description of brain responses and interactions with expression perception.

The aim of the first study (**Chapter 8**) was to replicate previous findings reported in the literature on expression processes in healthy controls (Eimer and Holmes, 2002; Morris et al., 1996; Calder et al., 1996) and to further characterize the temporal and neuroanatomical aspects of these processes and their interaction with perception. Subjects' expression perception was evaluated using a categorization task of the "morphed hexogen" expressions (Calder et al., 1996). These stimuli were chosen as they consider depicting more life-like expressions and hence might be more sensitive to detect differences in expression perception (Adolphs and Tarnel, 2004). In the brain imaging experiments responses to fearful expressions were compared to responses to neutral expressions measuring evoked potential responses (ERP) using EEG and BOLD response using fMRI. These expressions were chosen because the contrast between them was shown to elicit the strongest early ERP differential response (Kawaski et al., 2001; Eimer et al., 2003; Krolak-Salmon et al., 2004; Williams et al., 2004). The ERP analysis focused solely on early responses up to 250ms post stimuli presentation.

The second study (**Chapter 9**) tested expression processes in two types of temporal lobe epileptic patients: with (*lesion* group) and without (*intact* group) lesions to the amygdala while comparing them to healthy subjects (*control* group). Expression processes (measured as perception, and as brain responses) were tested using identical procedures as above. Two hypotheses were tested: the first relates to the fast expression route hypothesis, which predicts that early expression effects (fearful vs. neutral) would be attenuated for patients with damage to the amygdala (i.e. *lesion* group) compared to patients with an *intact* amygdala and healthy *controls*. The second hypothesis predicts involvement of the amygdala in expression perception (Adolphs et al., 1995), thus the *lesion* group is expected to be impaired in categorizing expressions compared to the *intact* and healthy *control* groups.

# CHAPTER 8:

## FEAR BIAS EFFECTS ON

## NEURONAL RESPONSES TO

## EXPRESSION.

---

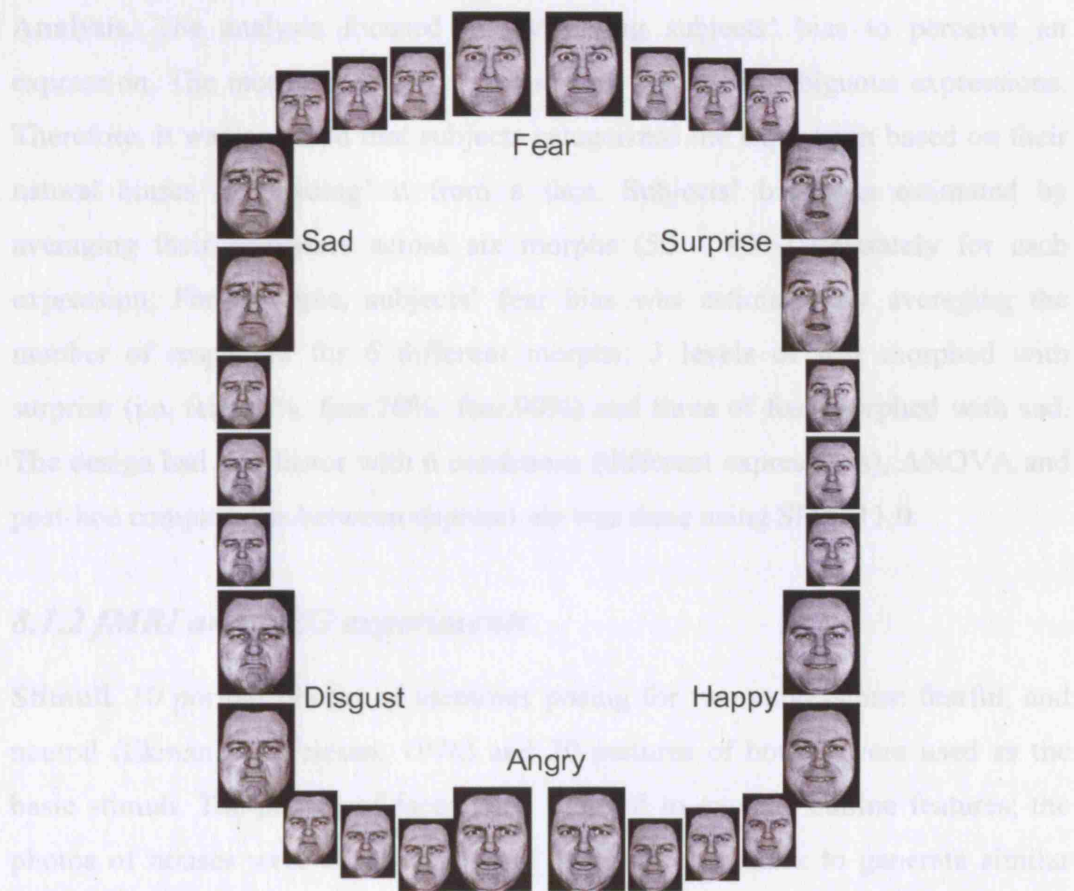
### 8.1 METHODS

**Subjects.** 15 healthy volunteers (8 females; mean age 34.5y; range 20 – 58y; 2 left handed) with no history of neurological or psychiatric illness participated in this experiment. Three volunteers did not participate in the expression categorization task due to technical problems; one of them did not participate in the EEG experiment due to time constraint. One other subject experienced claustrophobic feelings during the MRI scanning, and the experiment was aborted, though she did participate in the EEG and the behaviour sessions. All participants had normal or corrected to normal vision, and all gave written informed consent according to procedures approved by the Ethical Committee of the National Hospital for Neurology and Neurosurgery, London.

#### *9.1.1 Hexogen expression task*

**Stimuli.** 10 identities posing for the six basic prototypical expressions (i.e. fear, surprise, happy, angry, disgust and sad) taken from the Ekman and Friesen (1976) set were used. Faces were cropped to exclude outline features and were presented on a grey background. 6 identities depicting the prototypical expressions were

used for a practice session, a total of 36 stimuli. Morphed images of the remaining 4 identities were used in the main experiment. The morphed images were adapted from Calder et al. (1996). There were 6 levels of morphs in steps of 20%. Pairing of expression was based on a confusion matrix obtained from healthy volunteers (Calder et al., 1996). In the hexogen, expressions are morphed in the following order: fear-surprise-happy-anger-disgust-sad-fear. **Figure 8.1** presents the hexogen morph stimuli used for one identity. Each identity was morphed within itself. In total 120 morphs were used (4 identities \* 6 expressions \* 5 morph levels).



**Figure 8.1: Stimuli, hexogen expression task.**

Example of one identity in the hexogen expression matrix. Four different identities were used in the experiment. The prototypical expressions were morphed to generate five levels 20% distance apart (90-70-50-70-90) of mixture of expressions (Calder et al., 1996). The large images represent the 90% morphs.

**Procedure.** The experiment started with a practice session, where each of the six identities posing for the six prototypical expressions presented in random order with no time limit. The labels of the six expressions were numbered (1-to-6) and

presented below the image. The numbers assigned to the labels were random across subjects. Subjects were instructed to press the corresponding number for the expression that best described the image as accurately and quickly as possible. No feedback was provided. At the end of a practice session subjects were asked how comfortable they felt with the task and computer and could have another practise if wished. Three subjects chose to have another practice session. The main experiment followed the same procedure as the practice session, but with a different stimuli set. Each morph was presented twice in two separate sessions, with a short break in between (total of 240 morphs, 8 for each of the 30 levels).

**Analysis.** The analysis focused on evaluating subjects' bias to perceive an expression. The morphed nature of the stimuli provided ambiguous expressions. Therefore, it was assumed that subjects categorized the expression based on their natural biases in 'reading' it from a face. Subjects' bias was estimated by averaging their responses across six morphs (50 – 90%) separately for each expression. For example, subjects' fear bias was estimated by averaging the number of responses for 6 different morphs: 3 levels of fear morphed with surprise (i.e. fear.50%, fear.70%, fear.90%) and three of fear morphed with sad. The design had one factor with 6 conditions (different expressions), ANOVA and post-hoc comparisons between expressions was done using SPSS 11.0.

### ***8.1.2 fMRI and EEG experiments***

**Stimuli.** 10 portrait photos of identities posing for two expressions: fearful, and neutral (Ekman and Friesen, 1976) and 20 pictures of houses were used as the basic stimuli. The photos of faces were cropped to exclude outline features; the photos of houses were cropped as well using an oval mask to generate similar picture composition. Face stimuli were presented in two orientations: upright and inverted.

**Procedure.** A 2 (expression: neutral, fearful) by 2 (face orientation: upright, inverted) factorial design was used with an additional condition of houses. Stimuli were presented for 300ms with an SOA of 2500ms in a random order. The task was to detect (via a button press) an immediate repetition of a stimulus, which



could occur in any of the stimuli types with 15% chance i.e. one-back task. The experiment was divided into epochs (fMRI: 5, EEG: 8 epochs). In each epoch all stimuli were presented (60stimuli + ~10 target repetitions). At the end of each epoch subjects received feedback on their performance indicating their accuracy, reaction time and false alarms. The experiment started with a practice session, which was structured as an epoch and included presentation of all stimuli. This was done to familiarize the subjects with the set of stimuli used in the experiment and to minimize novelty effects. Subjects were instructed to fixate through out the experiment, to avoid head movements and to respond as quickly and accurately as possible. The order of the EEG and the fMRI experiments was counterbalanced across subjects. After the imaging session subjects performed the expression categorization task (see above).

**fMRI imaging and first level analysis.** A Siemens 1.5T Sonata system (Siemens, Erlangen, Germany) was used to acquire 26 oblique slices, 2 mm thickness, with 1.5mm gap with in-plane resolution of  $3 \times 3 \times 4.5 \text{ mm}^3$ , with 64\*64/ 900/ 50msec/ 2340sec (matrix/ FA/ TE/ TR), see **Chapter 2** for more details. Pre-processing included spatial realignment, unwrapping, slice time correction, normalization and smoothing (see **Chapter 2** for more details). The first-level design matrix included seven regressors depicting the onset of each event for the five experimental conditions (recall the  $2 \times 2 + 1$  design), with repetition events and feedback modelled separately. All these regressors were convolved with the canonical HRF (Friston et al., 1998).

**EEG recordings and first level analysis.** Recordings were made from Ag-AgCl electrodes using the NeuroScan system and the 10-20 montage system. 24 sites were recorded: Fpz, F7, F3, Fz, F4, F8, FC5, FC6, P7, C3, Cz, C4, P8, CP5, CP6, T5, P3, Pz, P4, T6, O1, O2 and Oz with linked-earlobe reference (see **Fig. 3.2**, electrodes marked in red). Horizontal EOG (HEOG) was recorded bipolarly from the outer canthi of both eyes (**Fig. 3.2** electrodes marked in green). Electrode impedance was kept  $< 5\text{k}\Omega$ . Amplifier bandpass was 0.1-40Hz. EEG and HEOG were sampled with a digitization rate of 200 Hz. EEG Recording followed Eimer and Holmes' (2002) procedures. Analysis implemented using SPM EEG (Wellcome Department, UCL, London). Preprocessing included epoching the data

from -100ms pre stimuli onset to +600ms post stimuli onset, artefact removal (epochs with more than 100mv were excluded from further analysis), no additional frequency filtering was applied to the data. Six event types were defined as 5 conditions (recall the design had a  $2 \times 2 + 1$  cells) and one repetition event. ERPs for each event were computed relative to the pre-stimulus base line (-100ms to 0). A threshold for artefact removal was set to 100mV that excluded events with eye blinks, lateral and vertical eye movements or any other artefacts due to movement or electrodes malfunction. In the first level analysis three post stimulus time windows were defined: ERP1, 110 – 150ms; ERP2, 155 – 200ms; ERP3, 205 – 250ms.

**The second level analysis** tested for consistent effects across subjects in a one sample t-test using contrast images (separate for EEG, fMRI) from the first level. The analysis focused on only three effects. A **face effect** was defined as the difference between faces *versus* houses and was used to verify existence of robust effects of face stimuli known in the literature. More importantly, an **expression effect** was tested by the comparison of upright fearful *versus* upright neutral expressions. Finally an **effect of fear bias** was tested as modulator of the **expression effect** by using a simple regression model.

## 8.2 RESULTS AND DISCUSSION

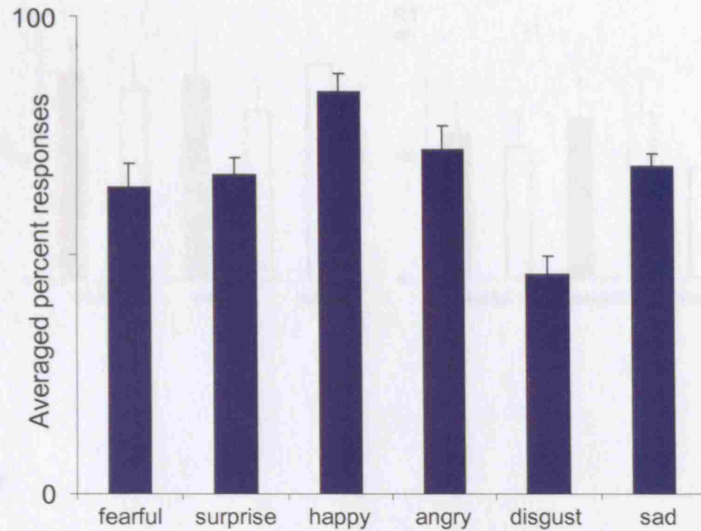
### 8.2.1 *Hexogen expression task*

Expression bias responses for each expression were estimated by averaging the number of responses to morphs that contained that expression (50% – 90%, see **8.1.1 Methods**). Results for the expression bias measure are presented in **Figure 8.2**, (see also **Fig. 9.2** for results for each morph level). There were significant differences in response bias between expressions ( $F_{5,55} = 11.9$ ,  $P < 0.001$ ) suggesting that different expressions had different negative or positive biases. A set of paired t-tests demonstrated a general negative bias to categorized disgust expression, such that disgust was less often categorized by subjects compared to all other expressions ( $P < 0.005$ ). A positive tendency to categorize happy

expressions, especially when compared to disgust, sad and surprise expressions ( $P < 0.005$ ) was also observed.

**Figure 8.2 Expression bias**

Percent responses for each expression averaged across 6 morphs levels that contained that expression. See 9.1.1 Methods for more details.



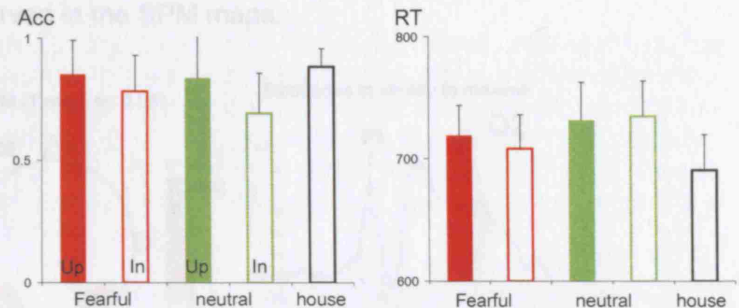
### 8.2.2 One-back task, behaviour results from the imaging experiments

There was no significant difference between the behaviour results of the fMRI and the EEG experiments, and therefore the results of these two experiments are collapsed. Results for accuracy and reaction times are presented in **Figure 8.3**. As expected, ANOVA with 2(expression) by 2(orientation) factors computed on accuracy responses revealed a main effect for orientation ( $F_{1,14} = 11.9$ ,  $P < 0.01$ ) supporting the idea that repetitions of upright faces are better detected than repetitions of inverted faces. This effect was not observed for reaction times. There was also a trend suggesting subjects were better at detecting repetition of fearful compared to neutral expressions ( $F_{1,14} = 4.23$ ,  $P = 0.059$ ) and this was evident for reaction times with faster responses for fearful compared to neutral expressions ( $F_{1,14} = 3.73$ ,  $P = 0.074$ ). No significant interaction was observed between expression and orientation. Importantly, the simple effects of interest in the following analysis of the imaging results (i.e. **Face effect**, face vs. house; **Expression effect**, fearful vs. neutral) did not differ in terms of task

performances. This suggests that any effects observed in the EEG or the fMRI cannot be accounted by task confounds.

**Figure 8.3: One back task**

On the left accuracy (Acc) presented as proportion of correct detection of repetition, on the right reaction time (RT) in msec. Error bars represent SEM. Up, upright face; In, inverted face



### 8.2.3 EEG experiment

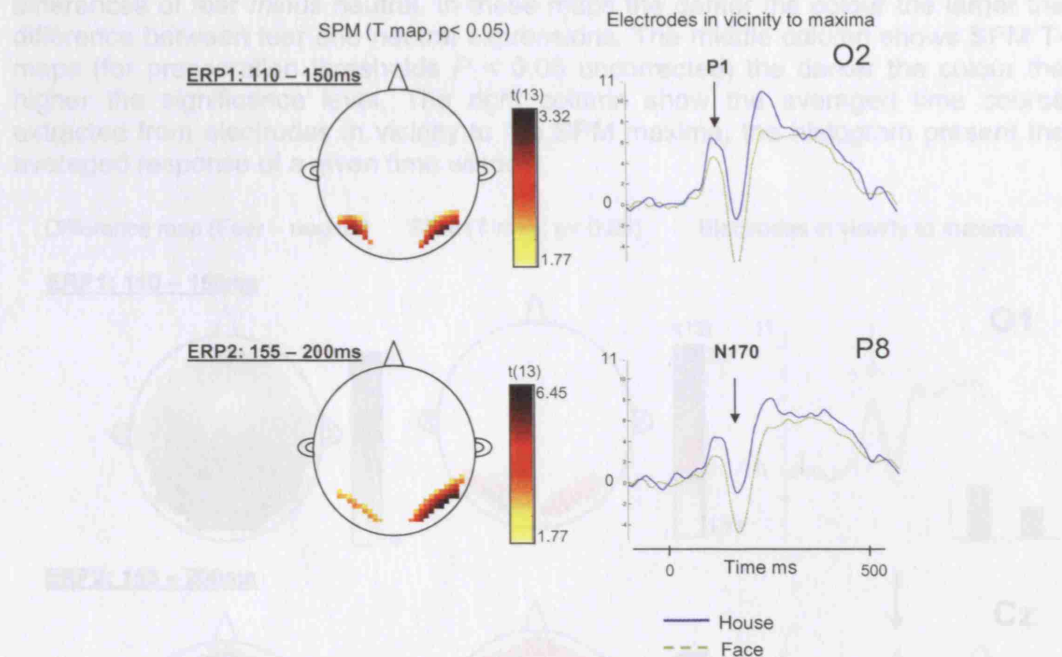
**Face effect** – a face effect was examined by comparing upright faces to houses in two time windows between 110 – 200ms (**Fig. 8.4**). An early differential effect was observed at ERP1 (110 – 150msec) in bilateral posterior electrodes stronger for left electrodes. The existence of this early P1 differential effect for faces compared to houses was reported recently by Liu et al. (2003).

As expected within ERP2 (155 – 200msec), an N170 effect was observed in bilateral posterior electrodes, with a more negative signal to upright faces compared to houses. This result replicates numerous studies (cf. Bentin et al., 1997; Eimer et al., 2001)



**Figure 8.4 Face effect**

On the left SPM T- maps from the second level analysis showing pixels with significantly larger negative wave for faces compared to houses (for presentation maps are threshold to 0.05 uncorrected) for the two time windows tested. On the right the averaged time course across subjects taken from electrodes (O2, P8) in vicinity to the maxima observed in the SPM maps.

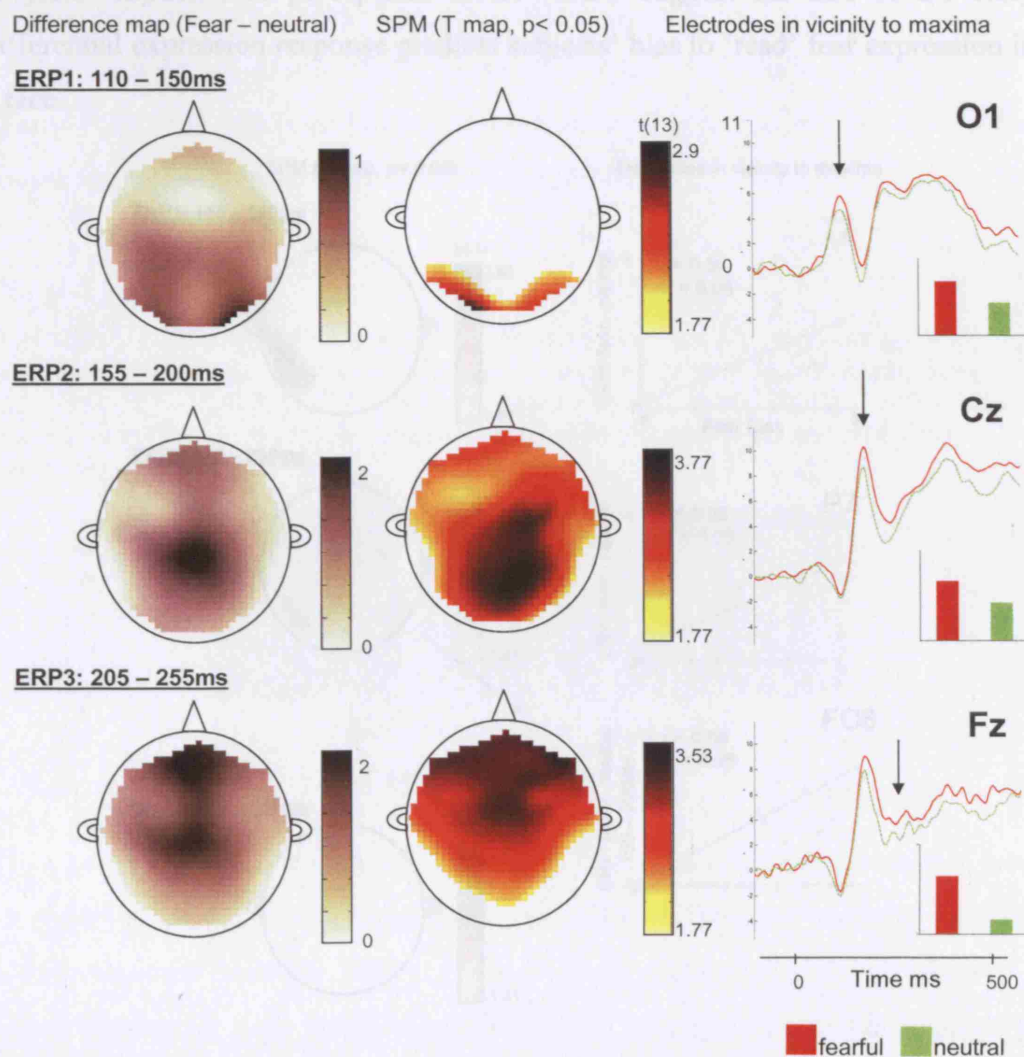


**Expression effects** – an expression effect was tested by comparing upright fearful to upright neutral faces at three early time windows from 110 to 250msec (**Fig. 8.5**). An early expression effect (ERP1, 110 – 150msec) was observed in posterior electrodes in an ERP component known as P1, with response for fearful more positive compared to neutral expressions. This replicates the effect observed by Eimer and Holmes (2002) in time and direction, but not in its spatial location. These authors observed this effect over frontal electrodes, while here the significant effect was in posterior electrodes. Note that this early expression effect occurs at the same time window as the early face effect, but in more medial electrodes than the face effect (which was in more lateral electrodes). In the two following time windows the expression effect propagated first to more anterior-medial electrodes, and then to anterior frontal electrodes with fearful faces always showing a more positive wave than neutral faces, replicating Eimer and Holmes (2002; Holmes et al., 2003). Note, that the expression effect in the second time window (155 – 200msec, **Fig. 9.5**) is not observed in the same electrodes

associated with the N170 face effect, replicating again Eimer and Holmes (2002) findings that show no expression effect at N170 peak electrodes.

**Figure 8.5: Expression effects**

On the left contrast images for the three time windows tested, representing the differences of fear *minus* neutral. In these maps the darker the colour the larger the difference between fear and neutral expressions. The middle column shows SPM T-maps (for presentation thresholds  $P < 0.05$  uncorrected) the darker the colour the higher the significance level. The right column show the averaged time course extracted from electrodes in vicinity to the SPM maxima, the histogram present the averaged response of a given time window.

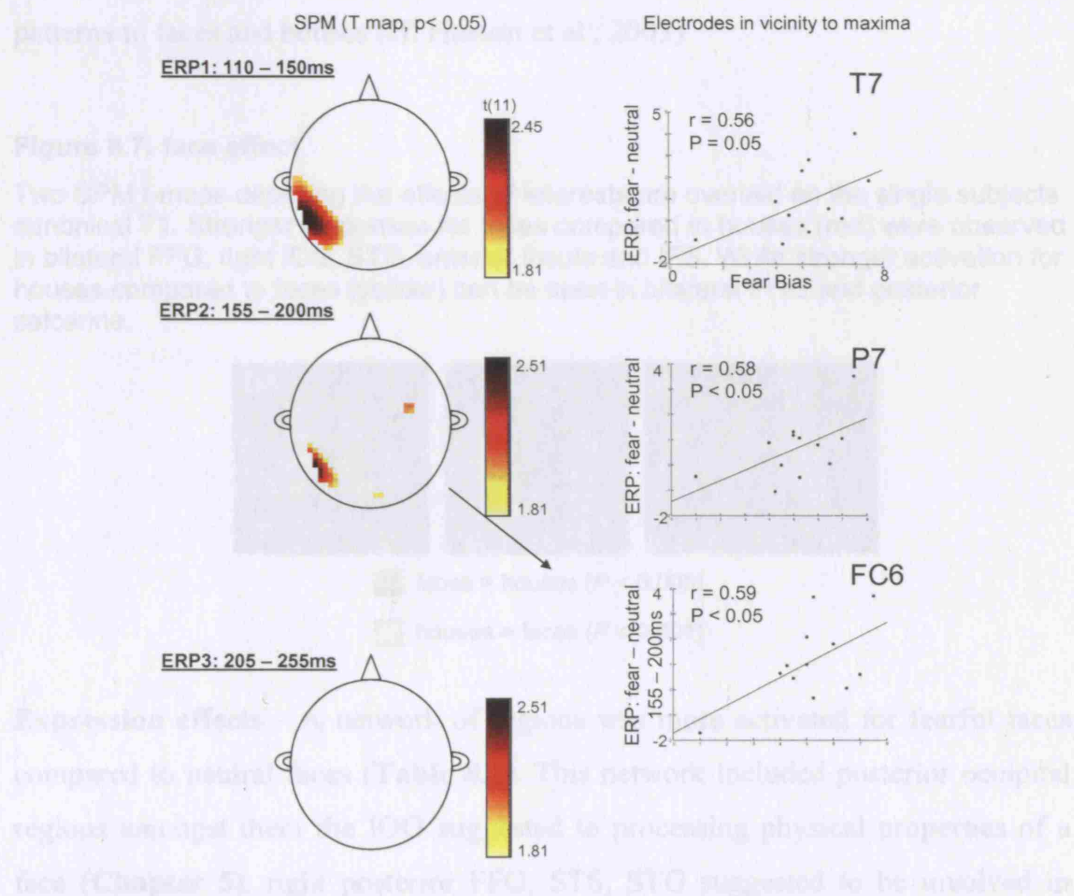


**Figure 8.5: Fear bias effects**

**Fear bias effects** - Finally, I tested the effect of subjects' fear bias on the size of their ERP expression effects. Recall that for each subject, an estimation of their tendency to perceive fear (i.e. fear bias) was calculated from the hexogen morph expression task (see above). Correlations were tested using a simple regression



analysis with subjects' fear bias as one variable and their ERP expression effect (i.e. fear – neutral) as a second variable, using a separate model for each time window. The early ERP expression effect (i.e. ERP1) positively correlated with subjects' fear bias (**Fig. 8.6**). This effect was seen in the left posterior lateral electrodes and continued till 200ms. There was no evidence for a correlation with fear bias in the latter time window tested i.e. between 205 - 250ms. Interestingly, even though the task in the current experiment was not directly related to the face expression manipulation (i.e. one-back task) early brain responses correlated with subjects' explicit fear perception. These results suggest the size of the early differential expression response predicts subjects' bias to 'read' fear expression in a face.



**Figure 8.6: Fear Bias effects**

On the left column SPM correlation maps for the three time windows tested (for presentation threshold to  $P < 0.05$  uncorrected). On the right scatter plots with the ERP effect of each subject (taken from electrodes in vicinity to the SPM maxima) plotted against his/her fear bias score. Note, that the third scatter plot represents ERP2 rather than ERP3. The difference in the statistic values between SPM (on the left) and the regression analysis (on the right) are due to different models used by SPM and SPSS.

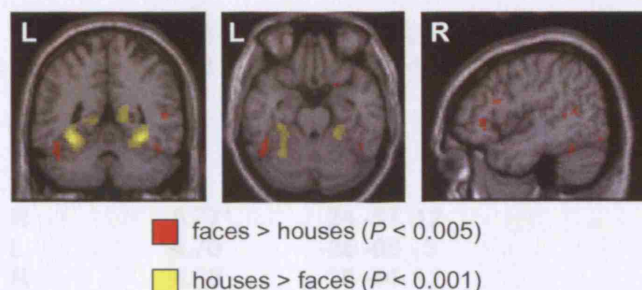


### 8.2.4 fMRI experiment

**Face effects (Table 8.1. and Fig. 8.7)** – As predicted a larger activation for faces compared to houses was observed in bilateral fusiform gyrus (FFG) a region that was labelled the fusiform face area (FFA; Kanwisher et al., 1997). Activation was also detected in additional regions suggested to be involved in face perception such as the right inferior occipital gyrus (IOG; possibly occipital face area, OFA), right superior temporal sulcus (STS), left middle occipital gyrus and left amygdala amongst others (Table 8.1). Houses showed a larger activation in bilateral parahippocampal gyrus (PHG) possibly reflecting activity in the region termed parahippocampal place area (PPA; Kanwisher et al., 1997) amongst other regions (Table 8.1). These findings replicate numerous studies that show similar response patterns to faces and houses (cf. Hasson et al., 2003)

**Figure 8.7: face effect**

Two SPM t-maps depicting the effects of interests are overlaid on the single subjects canonical T1. Stronger responses for faces compared to houses (red) were observed in bilateral FFG, right IOG, STS, anterior insula and IFS. While stronger activation for houses compared to faces (yellow) can be seen in bilateral PHG and posterior calcarine.



**Expression effects** – A network of regions was more activated for fearful faces compared to neutral faces (Table 8.2). This network included posterior occipital regions amongst them the IOG suggested to processing physical properties of a face (Chapter 5), right posterior FFG, STS, STG suggested to be involved in processing variant information from a face (Haxby et al., 2001) and especially expressions (Winston et al., 2004) and regions suggested to relate to attention monitoring – such as intraparietal sulcus (IPS) and superior frontal gyrus (SFG). Surprisingly the amygdala did not show the expected expression effect. Though, at a lower threshold ( $P < 0.005$ ) the peak of the thalamic activation extended into

the amygdala. The FFG gyrus activation was also weaker than expected and appeared only in the left hemisphere. The weaker effects observed in both these foci might relate to adaptation effects, as subjects were repeatedly exposed to the same set of faces (Brieter et al., 1996; Krolak-Salmon et al., 2004; Rotshtein et al., 2001).

**Table 8.1: Face effect (RFX t-test df = 13)**

Anatomy	H	Z	MNI (x,y,z)
---------	---	---	-------------

**a. upright faces > houses**

**Occipital**

Calcarine	R	4.94*	6 -81 15
IOG	R	3.22	48 -78 -15
MOG	L	3.09	-51 -75 12
FFG	R	2.67	48 -48 -27
	L	3.60	-45 -48 -27

**Temporal**

STS	R	4.17	60 -39 15
aTP	R	4.07	33 6 -33
aTP	L	3.27	-36 9 -30

**Frontal**

Ant. insula	R	3.40	48 33 3
	L	3.60	-36 39 3
IFG	R	3.09	51 15 21
SFG	L	3.02	-48 39 24

**Subcortical**

Amyg	L	2.78	-24 6 -21
SN	L	3.33	-9 -12 -18

**b. houses > upright faces**

**Occipital**

Calcarine	R	5.77*	24 -57 12
MOG	L	4.70	-36 -96 3
MOG	R	4.68	36 -84 12

**Temporal**

PHG	R	5.82*	33 -48 -12
PHG	L	5.48*	-33 -48 -12
aSTS	L	3.98	-63 -9 -6
aSTS	R	3.46	60 3 -6

**Frontal**

SFG	R	4.71	27 21 39
-----	---	------	----------

Abbreviations: IOG, inferior occipital gyrus; MOG, middle occipital gyrus; FFG, fusiform gyrus; STS, superior temporal sulcus; aTP, anterior temporal pole; Ant. Anterior; IFG, inferior frontal gyrus; SFG, superior frontal gyrus; Amyg, amygdala; SN, substantia nigra; PHG, parahippocampal gyrus; aSTS, anterior STS; L, left; R, right. \*  $P < 0.05$ , correct for whole brain voxel level.

**Table 8.2: Expression effect (RFX t test df = 13)***Upright: fearful > neutral*

Anatomy	H	Z	MNI (x,y,z)
<b>Occipital</b>			
Calcarine	M	4.36	9 -87 0
Cuneus	M	3.46	6 -87 15
IOG	R	3.42	33 -87 -24
pFFG	L	3.59	-42 -63 -24
<b>Temporal</b>			
STS	R	4.09	42 -27 -9
STG	R	3.11	63 -24 0
MTG	L	4.74	-57 -15 -15
<b>Parietal</b>			
IPS	R	3.47	36 -48 45
<b>Frontal</b>			
Insula	R	4.03	33 33 0
SFG	R	3.57	21 36 39
	L	3.26	-36 42 21
<b>subcortical</b>			
Thalamus	R	3.36	18 0 -9
Hipp	R	3.16	39 -21 -15
Hipp	L	2.88	-36 -15 -24

Abbreviations: IOG, inferior occipital gyrus; pFFG, posterior fusiform gyrus; STS, superior temporal sulcus; STG, superior temporal gyrus; MTG, middle temporal gyrus; IPS, inferior parietal sulcus; SFG, superior frontal gyrus; Hipp, hippocampus; M, medial; R, right; L, left.

**Fear bias effect** – A network of cortical regions positively correlated with subjects' fear bias (**Table 8.3**). The strongest effects were observed in the bilateral superior frontal gyrus (SFG, **Fig. 8.8**). Positive correlations were observed as well in bilateral STS supporting their role in processing expressions (Winston et al., 2004). Interestingly, positive modulation of the right post-central sulcus (post-CS, i.e. S1) and right insula by subjects' fear bias was also observed. Involvement of the right post-CS and insula is in accordance with results reported by Adolphs et al. (2000) that show lesions to these regions correlated with impaired expression perception.

**Table 8.3: Fear bias & Expression effect (RFX, df = 10)****Positive correlation fear bias & [Up.fear – Up.neutral]**

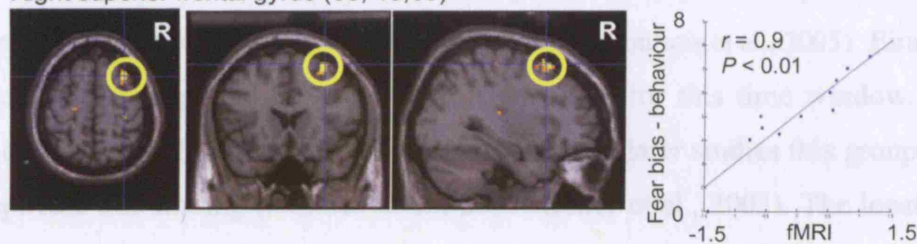
Anatomy	H	Z	MNI (x,y,z)
<b>Occipital</b>			
Calcarine	L	3.55	-12 -63 15
precuneus	R	3.52	6 -63 51
<b>Temporal</b>			
STS R	3.43	45 -33 6	
pSTS R	3.36	42 -75 33	
L	3.16	-42 -69 42	
<b>Parietal</b>			
IPS L	3.41	-24 -66 24	
<b>Frontal</b>			
SFG R	4.10	33 18 60	
	3.41	36 -6 57	
L	3.66	-24 39 48	
Post CS	R	3.78	48 -30 51
CS R	3.29	33 -27 60	
L	3.52	-21 -18 57	
Insula R	3.19	-30 24 3	
OFC L	3.81	-36 36 -21	
CG R	3.33	18 -45 36	

Abbreviations: STS, superior temporal sulcus; p, posterior; IPS, inferior parietal sulcus; SFG, superior frontal gyrus; CS, central sulcus; OFC, orbital frontal cortex; CG, cingulate gyrus; R, right; L, left.

**Figure 8.8: fear bias effects**

On the left, SPM simple correlation map (threshold  $P < 0.001$  uncorrected) overlaid on a canonical T1 image. On the right, scatter plot of the between the fMRI expression effect size extracted from the maxima marked in yellow circle and subjects' fear bias.

Right superior frontal gyrus (33, 18, 60)



### 8.3 DISCUSSION

The aims of this study were to replicate previous findings of brain responses to face and facial expression and to test for modulation of these effects by subjects' fear bias. In the EEG study, a differential expression effect was observed already between 110 – 150ms after stimuli presentation. This early effect predicted subjects' fear bias, namely their tendency to perceive an ambiguous expression as fearful. In the fMRI study, I replicated the network for fearful expression observed previously (Morris et al., 1998; Passoa et al., 2002). This network included early visual cortices such as calcarine, precunues as well as extrastriate regions such as the IOG, FFG and STS and right insula (**Table 8.2**). More interestingly, the size of the fear expression effect in the calcarine sulcus, right STS, posterior central sulcus (post-CS), insula and SFG predicted subjects' fear bias (**Table 8.3**).

The very early ERP effects observed here (**Fig. 8.4**) are supported by single cell recordings in monkeys that show the amygdala differential expression response at latencies of 110 – 200msec (Leonard et al., 1989), and in humans where an early differential expression effect (120 – 160msec) was observed in prefrontal cortices (Kawaski et al., 2001). However, not all studies have observed such an early differential response in the amygdala (Krolak-Salmon et al., 2004). Using scalp electrophysiology, an early (start just after 100msec) MEG differential response to expression was observed by Streit et al. (2003). Interestingly, they localize the sources of this effect to the amygdala, posterior occipital regions and frontal regions. This raises the possibility that an early brain response (after 100ms) to expression involves a network of regions rather than a single structure.

Other studies have shown differential P1 responses for fearful compared to neutral faces in posterior electrodes (Williams et al., 2004; Pourtois et al., 2005). Eimer and Holmes (2002) reported an early expression effect for this time window, but it was only significant in frontal electrodes, though, in later studies this group failed to replicate this finding (Holmes et al., 2003; Eimer et al., 2003). The location of the expression effect observed in their first study (Eimer and Holmes, 2002) i.e. N1, frontal electrodes is inconsistent with the current study where the early

expression effect was observed mainly in posterior electrodes. It is hard to account for the inconsistencies between the two studies regarding the spatial distribution of the early expression effect (ERP1). Despite, this inconsistency, the direction of the expression effect in both studies was similar with fearful faces showing a more positive wave compared to neutral. This was observed here across all electrodes (**Fig. 8.5**).

The expression effect observed here continued until 250ms, where fearful expressions elicit a more positive wave compared to neutral expressions (**Fig. 8.5**). This is consistent with intracranial recordings where it was demonstrated that the expression effect in the amygdala persisted up to 1300 msec, and propagated in this time window to occipital-temporal and frontal regions, i.e. (IOG, MOG), STS, MTG and OFC (Krolak-Salmon et al., 2004). Studies using scalp recordings observed similar expression effects in these later time windows (Sato et al., 2001; Batty and Taylor, 2003, Streit et al., 2003; Eimer et al., 2003) but not all (Eimer and Holmes, 2002). Eimer and Holmes (2002) did not observe an expression effect between 205 – 250msec, as I observed here, but only up to 200msec.

**Modulation of expression effect by subjects' fear bias** – Here, I used the natural variability of the healthy population in responses to fearful expression to reveal a neural correlation that might account for such differences. Interestingly, the early ERP expression effect (P1) predicted subjects' fear bias, Thus as the differential expression response was larger, subjects' fear bias was stronger. The effect of the fear bias was attenuated with time and abolished after 205ms. This might be due to the fact that this information was irrelevant to the task (one back task).

Neural correlates of subjects fear bias were observed in the fMRI experiment as well (**Table 8.3**), where a larger expression effect correlated with larger fear bias in the calcarine, STS, post-CS, insula and SFG amongst other regions. The involvement of STS in predicting subjects' fear bias is consistent with its role in processing expression (Haxby et al., 2000; Winston et al., 2004). The involvement of post-CS and insula in processing expression was suggested by lesion studies (Adolphs et al., 2000).

Intriguingly, the current study failed to observe a strong differential expression response in the amygdala (Table 9.3), although the amygdala did show a significantly larger response to faces compared to houses. As mentioned above, the lack of differential expression effect in the amygdala might have resulted from adaptation of the fear signal, as the amygdala response has been shown to be affected by long-term adaptation (Brieter et al., 1996). This adaptation may arise as an attenuation of feedback input. Recall that the fMRI BOLD response (Chapter 2) is suggested to represent mostly local field potentials (i.e. the input to a region, rather than its output). Thus, one interpretation of the results is that the amygdala receives information about all faces. It also processes facial expressions and in case of fear the amygdala projects this information to other cortical regions. Thus, lack of a differential expression signal in the amygdala does not imply that it is not involved in fear processing. The most straight-forward way of establishing the role of the amygdala in processing expression is to test the effects of amygdala lesions on differential expression response in the brain. This is the aim of the next study.



# CHAPTER 9:

## AMYGDALA ROLE IN EARLY EXPRESSION PROCESSING

---

In **Chapter 8**, an early ERP (P1) differential response to expressions was observed for healthy subjects. Furthermore the size of this effect predicted subjects' fear bias responses. This rapid differential response to expression offers support to the fast route hypothesis for fearful expression processing and suggests that input from this route contributes to perception of fearful expressions. However, the fast route hypothesis also predicts that expression processing is mediated via the amygdala. Intriguingly, in the fMRI results I did not observe robust differential amygdala response to expressions and its responses also did not relate to subjects' fear perception. Therefore, to directly test the role of the amygdala in expression processing, I compared brain and behaviour responses of patients with lesions to the amygdala to those with intact amygdala. The chapter addresses two questions: the first relates to the role of the amygdala in perceiving expressions; the second relates to the contribution of the amygdala to expression effects observed in healthy brain responses, as measured by ERP and fMRI.

### 9.1 METHODS

**Subjects.** 17 temporal lobe epileptic patients participated in the experiment. All were diagnosed as part of a clinical evaluation for epilepsy. Importantly, none have undergone any brain surgery. Diagnoses were provided by Dr. M. Richardson from the Epilepsy Unit, National Hospital for Neurology and

Neurosurgery, London, and was as follow: 7 patients with amygdala *lesions* (4 female, mean age 34y, range 21 – 40y, 2 left handed); 10 patients with *intact* amygdala (5 females; mean age 37.5y; range 23 – 48y; 2 left handed; for more details see **Table 9.1**). The two patient groups did not differ significantly in their I.Q. scores (WAIS-R:  $t_{13} = 1.7$ ,  $P = 0.1$ ; WAIS-RP:  $t_{13} = 1.4$ ,  $P = 0.2$ ), epilepsy onset ( $t_{15} = 0.9$ ,  $P = 0.37$ ), frequency of seizures ( $t_{10.67} = 1.2$ ,  $P = 0.28$ )<sup>1</sup>, or the amount of medication taken per day ( $t_{9.16} = 1.4$ ,  $P = 0.2$ ). The healthy controls were the subjects that I report above (**Chapter 8**). Patients and healthy *controls* were matched in age and socioeconomic background (i.e. most healthy *controls* were relatives and friends of the patients). One patient from the *intact* group did not participate in the behaviour experiment due to time constraints. All participants had normal or corrected to normal vision, and all gave written informed consent according to procedures approved by the Ethical Committee of the National Hospital for Neurology and Neurosurgery, London.

**Table 9.1: Patients details**

Patient number	Lesion	Aetiology	Age years	Onset years	Frequency GM PM	Medication Mg PD	WAIS-R I.Q.	WAIS-R PI.Q.
13	L H	MTS	47	3	1	1475	110	139
15	L HA	MTS	37	3	7	3400/2000	84	99
16	L HA	MTS	37	1	0.02	1600	94	93
17	L HA	MTS	42	10	6	850	104	108
18	L HA	MTS	21	0.5	7	2000	120	128
19	L HA	MTS	39	11	0.08	650	83	90
20	L H	MTS	40	7	1	335	76	88
22	L H	MTS	33	11	3	6600	74	68
23	L H	MTS	28	2	2.5	800	89	99
24	L H	MTS	36	6	35	4350	87	89
26	L H	MTS	42	3	1	2250	86	84
27	R A		34	17	0	500	116	124
28	L A		33	17	2	1200	-	-
29	TLE		33	0	30		-	-
30	L H	MTS	46	3	1.5		88	80
31	L H	MTS	23	10	2.5	3000	96	106
33	L H	MTS	48	14	2.5	1000	92	89

Abbreviations: GM, Grandmal; PM, per month; PD, per day; L, left; R, right; H, hippocampus; HA, hippocampus+amygdala; TLE, temporal lobe epilepsy lesion unspecified; MTS, medial temporal sclerosis.

**Procedure and analysis.** Importantly, the experimenter was blind to the specific patient diagnosis of the patients; diagnoses were obtained only for the analysis. The experimental design, procedures and analysis (at a subject level) for all three

<sup>1</sup> Comparison is corrected for unequal variance between groups.

experiments (behaviour, fMRI, EEG) were identical to the one reported above for the healthy *controls* (see 9.1 Methods).

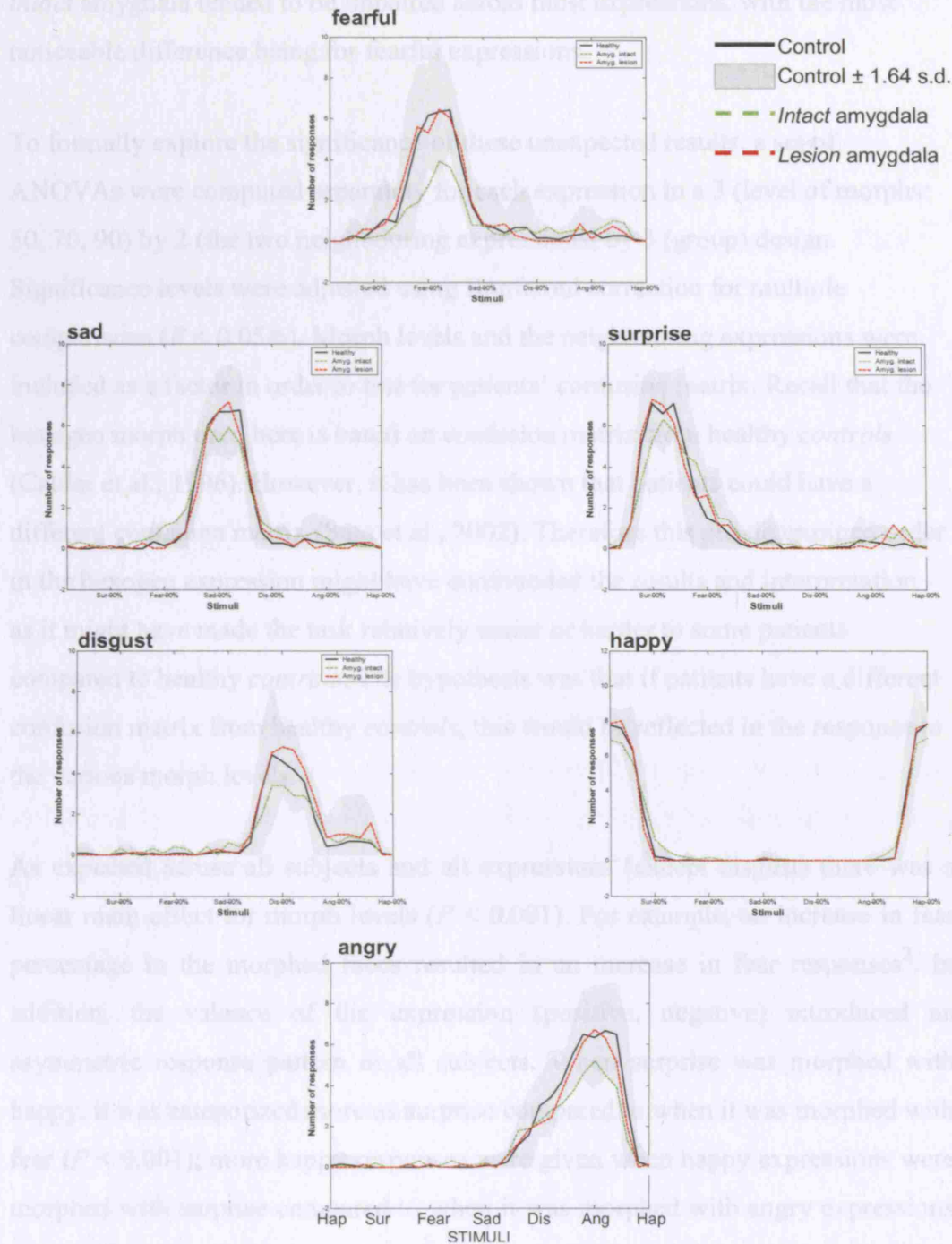
## 9.2 RESULTS

### 9.2.1 *Hexogen expression task*

Response biases were estimated as the average number of responses across six morphs (50-90%) around an expression (see above). Comparison of response biases for different expressions (6 expressions) and groups (3 groups) revealed a main effect of expression ( $F_{5,125} = 44$ ,  $P < 0.001$ ) but no main effect for group and no interaction of group and expressions.

A set of post-hoc t-tests showed that perceptions of happy expressions differ significantly from all other expressions, as participants tended to ‘read’ more happiness in an expression compared to all other expression categories ( $P < 0.0001$ ). Disgust expressions were more likely to be mislabelled compared to angry, sad ( $P < 0.0001$ ) and fear ( $P < 0.05$ ). Note that the results here for all subjects are different from the results reported for the healthy controls on their own (see 9.2.1). The main differences are in the biased responses for happy expressions, which were enhanced with the addition of the patients. Surprisingly, lesion site did not affect expression biases. Thus a lesion to the amygdala did not affect patients overall expression biases. The a-priori hypothesis suggested that such effects would be evident for a particular expression and especially in responses to fearful expression. I next examine each expression on its own.

**Figure 9.1** presents the pattern of responses for each group separately for each response. The grey area in the plots depicts 1.64s.d, i.e. 95% confidence interval around the averaged responses of the healthy *controls*. As expected, subjects were accurate in reading an expression conveyed by a morphed face, as responses for a given expression peaked when presented with a face that contained that expression. Moreover, the responses for a given expression gradually increased in a manner that depended on the percent of that expression in a morphed face.



**Figure 9.1 Hexogen expression task – response pattern**

The plots are organized based on the hexogen expression-morph (**Fig. 8.1**) in each graph only one response is plotted for all the different morphs (labelled at the top left), the stimuli labels are given in the x-axis of the angry response (bottom). The averaged responses of the healthy *control* are in black with 95% confidence interval around it - the grey area. Averaged responses of patients with a lesion to the amygdala are in red and for patients with intact amygdala in green.

Unexpectedly, the plots suggested that patients with a *lesion* to the amygdala categorize expressions in a similar way to healthy *controls*, while patients with

*intact* amygdala tended to be impaired across most expressions, with the most noticeable difference being for fearful expressions.

To formally explore the significance of these unexpected results, a set of ANOVAs were computed separately for each expression in a 3 (level of morphs: 50, 70, 90) by 2 (the two neighbouring expressions) by 3 (group) design. Significance levels were adjusted using Bonferroni correction for multiple comparisons ( $P < 0.05/6$ ). Morph levels and the neighbouring expressions were included as a factor in order to test for patients' confusion matrix. Recall that the hexogen morph used here is based on confusion matrix from healthy *controls* (Calder et al., 1996). However, it has been shown that patients could have a different confusion matrix (Sato et al., 2002). Therefore this pre-determined order in the hexogen expression might have confounded the results and interpretation - as it might have made the task relatively easier or harder to some patients compared to healthy *controls*. The hypothesis was that if patients have a different confusion matrix from healthy *controls*, this would be reflected in the response to the various morph levels.

As expected across all subjects and all expressions (except disgust) there was a linear main effect for morph levels ( $P < 0.001$ ). For example, an increase in fear percentage in the morphed faces resulted in an increase in fear responses<sup>2</sup>. In addition, the valance of the expression (positive, negative) introduced an asymmetric response pattern in all subjects. When surprise was morphed with happy, it was categorized more as surprise compared to when it was morphed with fear ( $P < 0.001$ ); more happy responses were given when happy expressions were morphed with surprise compared to when it was morphed with angry expressions ( $P < 0.001$ ). Finally, more angry responses were given when angry expressions were morphed with disgust compared to when it was morphed with happy. This suggests that valance is an important component in the confusion matrix, with subjects tending to confuse less between expressions when they convey similar

---

<sup>2</sup> Note, that such results suggest that expression perception is not categorical as others have argued (Lowrence et al., 1995) but linear. It might be that the categorical nature of results observe for expressions is due to task confounds i.e. two alternative force choice used in other experiments (see chapter 4) and do not reflect the nature of representation in the brain.

valence. Note, that both patient groups showed similar valence asymmetry when categorizing the morphed faces.

More importantly, there was a significant group effect for fearful expressions ( $F_{2,25} = 7, P < 0.005$ ), but surprisingly, tests for simple effects revealed that the group that had a different perception bias was the *intact* amygdala group. They labelled fewer expressions as fear compared to the amygdala *lesion* group ( $F_{1,15} = 10.5, P < 0.005$ ) and the healthy *controls* ( $F_{1,19} = 22.1, P < 0.001$ ). There were no significant differences between the amygdala *lesion* group and the healthy *control* ( $F_{1,16} = 0.11, P = 0.73$ ). Contrary to my hypothesis, patients with *intact* amygdala showed a different pattern of response from patients with *lesions* to the amygdala and healthy *controls*. Similar results were obtained even when the patients with non-MTS diagnosis were excluded (i.e. p27, p28, p29).

The fact that a *lesion* to the amygdala did not affect expression categorization is intriguing. Even more surprising is that patients with an *intact* amygdala were impaired in categorizing fear expression compared to patients with an amygdala *lesion* and healthy *controls*. A set of correlation analyses revealed that neither of the following factors predicted patients' fear bias: I.Q. scores, age of epilepsy onset, frequency of seizures, and amount of medication predicted patients fear bias<sup>3</sup>. To better understand the data, I explored it more carefully by examining individual responses. Each subject was compared to the mean response bias of the healthy *control* group. Outlier behaviour was defined if responses were more than 2s.d. from the mean of the healthy *controls* and a tendency for outlier behaviour was 1.5s.d from the mean of healthy control. I explored the estimated bias responses separately for each expression (**Fig. 9.2** and **Table 9.2**).

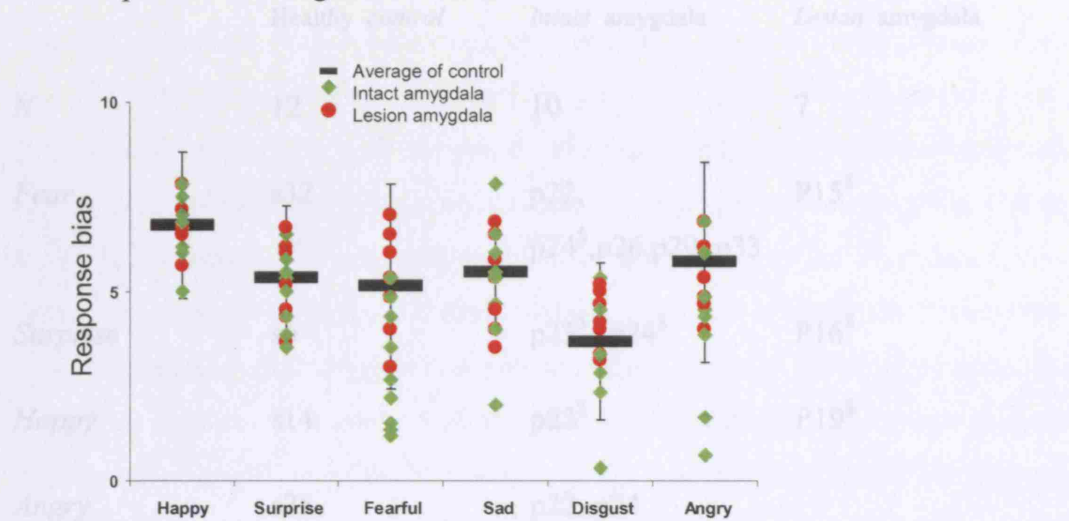
Outlier response pattern was observed for all expressions and within all groups. A number of points are worth noting in this regard. Firstly, four healthy *controls* exhibited outlier bias responses each for a different expression (**Table 9.2**). This suggests that within the healthy population different individuals have different

---

<sup>3</sup> Interestingly, as patients suffer from more frequent seizures (recall most left temporal epileptic) and took more medications they had larger positive bias in 'reading' happy in expressions ( $r = 0.54, P = 0.02$ ;  $r = 0.79$ ;  $P < 0.001$ , respectively).



biases in 'reading' an expression of a face. Thus, pointing to a potential problem for false positives in single case studies.



**Figure 9.2: Outliers behaviour**

The response bias of each individual patient (a circle) is plotted for each expression. The black line represents the averaged response bias of the healthy *control*, the error bars are  $2 \times \text{STDEV}$ . Green diamonds are patients with an *intact* amygdala and in red circles patients with an amygdala *lesion*. Any patient whose responses do not overlap the error bar is considered outlier.

Secondly, three patients within the *intact* amygdala group (p22, p23, p24) showed unspecified general outlier behaviour with negative biases to recognize three or more expressions. This might suggest that these patients have a more general bias in misreading the expression of a face, rather than a specific deficit with one expression. These patients had a relatively low I.Q. score (see Table 10.1).

Thirdly, two patients with a *lesion* to the amygdala (p18, p28) showed outlier negative bias for sad response, tending to perceive expressions as less sad than healthy *controls*, while one (p16) showed a positive bias tending to 'read' more sadness in expressions compared to healthy *controls*. This accords with recent report of abnormal perception of sad expressions in patients with amygdala lesions (Adolphs and Tarnel, 2004). Overall, six participants had an outlier response to sad expressions, though with inconsistent tendencies: two showing positive biases and four negative biases. This suggests that among the stimuli used here sadness was constituted the most ambiguous expression.



**Table 9.2: Outlier analysis – hexogen expression task**

	Healthy <i>control</i>	Intact amygdala	Lesion amygdala
<i>N</i>	12	10	7
<i>Fear</i>	s32	p22, p24 <sup>s</sup> , p26, p29, p33	P15 <sup>s</sup>
<i>Surprise</i>	s6	p23 <sup>s</sup> , p24 <sup>s</sup>	P16 <sup>s</sup>
<i>Happy</i>	s14	p23 <sup>s</sup>	P19 <sup>s</sup>
<i>Angry</i>	s25	p22, p24	
<i>Disgust</i>	s6	p23	
<i>Sad</i>	s10 <sup>s</sup>	+p22, p24, p23	+p18, p16, p28

Outlier response biases were determined as being < 2 s.d. different from averaged number of responses of the *control* group. <sup>s</sup>Performances <1.5 different from the *control* group. When specify '+' indicates a positive bias in labelling the expression compared to healthy *control*. In all other cases the bias is negative, i.e. a tendency to label the expression less than healthy *control*. "p" for patient, the numbers correspond to the number in Table 10.1, "s" for healthy *control* subjects, the numbers indicate the different individuals.

Responses to fearful expression were most vulnerable to negative outlier behaviour, with a total of five outliers and two tendencies toward an outlier biases. This is an intriguing result, though often observed in the literature (Adolphs et al., 1996). Given the ecological saliency that is attributed to fearful expression (Darwin, 1872) it is not clear why so many of us tend not to 'read' fear in a face. One possible way to resolve this apparent paradox is to assume separate processes for explicit recognition of fear and for autonomic and neuronal preparations for a potential threat situation arising from a fearful expression (Morris et al., 1998) as suggested by the dual route hypothesis (LeDoux, 1986, 1996).

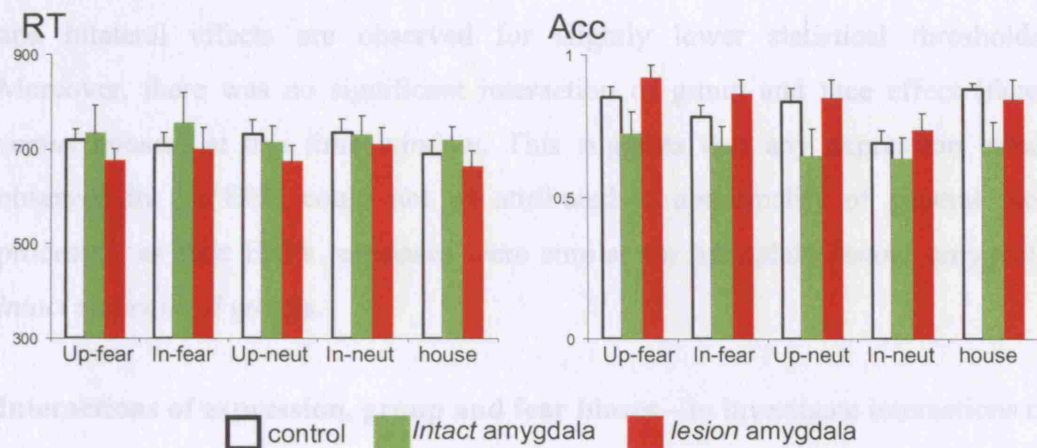
The outlier analysis suggests that the impairments observed in fear recognition for the *intact* group cannot be attributed to a single outlier, as half the patients from that group showed outlier behaviour or a tendency towards outlier biases. This result is not easy to explain, though a few possible explanations can be ruled out. It cannot be associated with lesions to the hippocampus as most patients had lesions that included the hippocampus whether in the *intact* or *lesion* group (Table 10.1). It cannot be attributed to the extent of the lesion, as the amygdala *lesion* group had a larger lesion spread than the *intact* group. It was not associated with patients' general intellectual ability (measured as I.Q), age of onset of epilepsy, frequency of seizures or amount of medications. Other factors that might account for this result might relate to the lifestyle of the patients, their social intelligence etc. Thus more research needs to be done to clarify this issue.

To summarize, different expression biases existed in the healthy *control* group and in both patient groups. There was no obvious association between lesion location and perception biases. The finding that response biases of 12 out of 31 participants was characterized as outlier behaviour given a conventional cut off point ( $< 2s.d.$ ) stresses the risk in case studies and of drawing strong conclusions on function-anatomy relation from single cases. The results demonstrated that there is variability in subjects' expression biases. Therefore, in the follow up analysis, fear bias measure was used as covariate. This enabled me to dissociate between effects of subjects' fear bias and effects of malfunctioning amygdala due to lesion.

### **9.2.2 One-back task**

The task in the EEG and fMRI experiments was one-back, where subjects were instructed to detect an immediate repetition of a stimulus (see 9.1.2 Methods). Recall, the design had 2 (expression) by 2 (orientation) factors *plus* the houses condition. Here in the analysis an additional factor of 'group' was added. Significant effects were only observed in response accuracy, though similar patterns can be seen in reaction times. As expected, there was a significant effect of orientation ( $F_{1,29} = 18.324$ ,  $P < 0.001$ ), with more repetitions detected for upright than inverted faces. There was also a significant effect of expression ( $F_{1,29}$

= 18.324,  $P < 0.001$ ) with higher accuracies for detecting repetition of fearful than neutral expressions. Here, as opposed to the healthy *controls*, repetitions of fearful upright faces were better detected than that of upright neutral faces ( $F_{1,29} = 5.7$ ,  $P < 0.05$ ). There was no significant effect of group, although inspecting the results (**Fig. 9.3**) the *intact* amygdala group appeared slower and less accurate than the amygdala *lesion* and healthy *control* groups on all stimuli types. This group effect was not significant and was mainly due to one outlier (p26). The rest of the patients in the *intact* group performed within the normal range. There were also no correlations between fear bias and expression effect observed in subjects' behaviour responses in the one-back task. This suggests that any interaction between group or fear bias with expression in the EEG and fMRI results can not be accounted by task confounds.



**Figure 9.3 One back task**

Reaction time (RT) and accuracy (Acc) results for the task performed during the EEG and fMRI experiments. Up, upright faces; In, inverted faces. Error bar represent SEM.

### 9.2.3 EEG experiment

A **face effect** was investigated by comparing upright faces vs. houses for the two early time windows, separately for each group. In the first time window (110 – 150ms) both groups showed a more positive response to houses compared with faces, although the *intact* amygdala group showed this effect in frontal electrodes for the component N1, while the amygdala *lesion* group showed this effect in

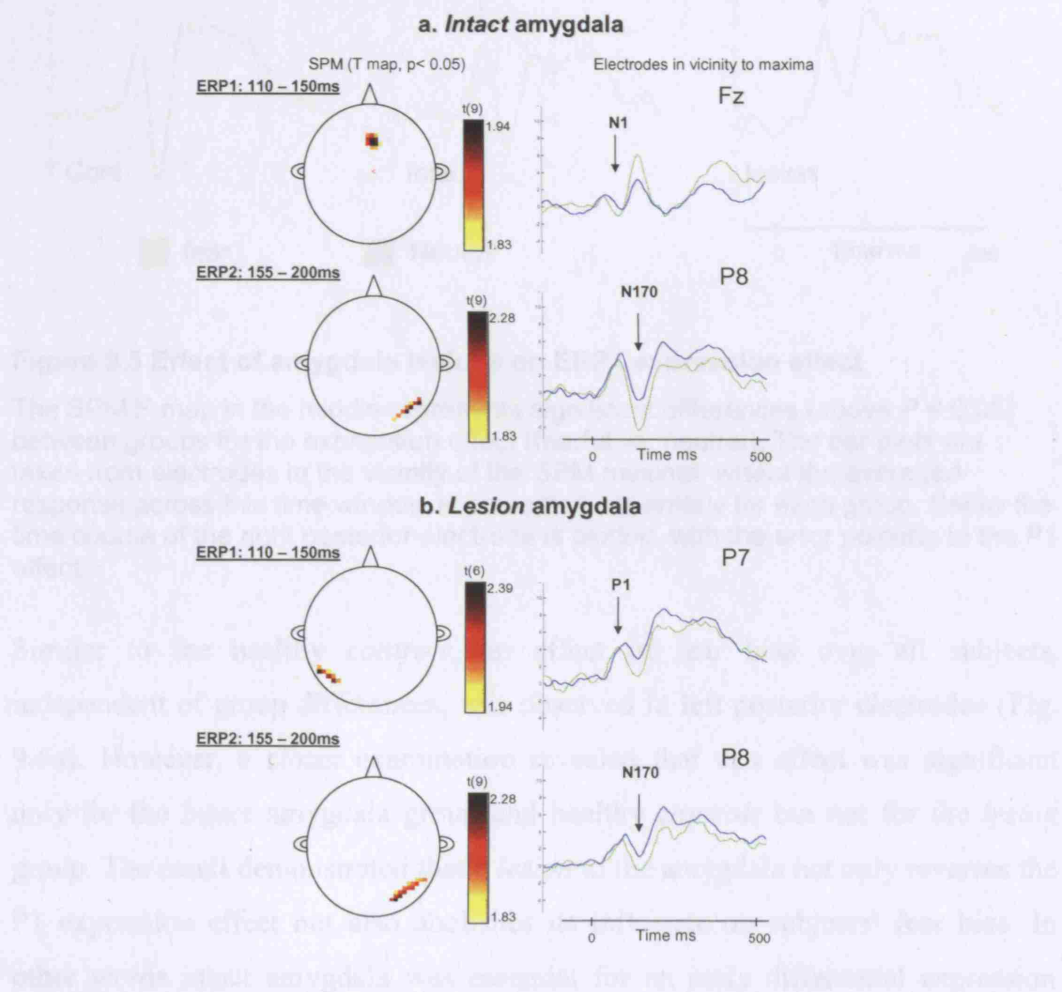
lateral posterior electrodes for P1. Recall that the healthy *controls* showed this effect in lateral posterior electrodes (i.e. P1, **Fig. 8.4**) similar to the amygdala *lesion* group and not to the *intact* group. A direct comparison revealed no significant interaction of face effect and groups in this time window. The inconsistent results might relate to the small number of subjects within each group that reduces statistical power. Importantly, these results suggest that the early (ERP1) differential face effect was not related to amygdala abnormality.

As expected more robust effects were obtained in the second time window, where both patient groups showed N170 (155 – 200msec) face effect in right lateral posterior electrodes, with faces eliciting more negative responses than houses. As opposed to healthy *controls*, in both patients groups the effect was unilateral rather than bilateral, but a closer inspection revealed that this is a threshold issue and bilateral effects are observed for slightly lower statistical thresholds. Moreover, there was no significant interaction of group and face effect (faces *versus* houses) at this time window. This suggests that any expression effect observed in the EEG could not be attributed to abnormality of general face processes, as face ERPs responses were similar for amygdala *lesion*, amygdala *intact* and *control* groups.

**Interactions of expression, group and fear biases** – to investigate interactions of expression and group an ANCOVA model was designed separately for each time window of interest, with expression effect (fearful – neutral) being the dependent variable, group as a three level factor (*control*, *intact*, *lesion*) and subjects' fear bias was a parametric covariate.

As the fast expression route hypothesis predicts, epileptic patients with amygdala *lesion* differed from patients with *intact* amygdala and from the healthy *controls* at the very early ERP component P1, i.e. 110 – 150ms after stimulus presentation (**Fig. 8.5**). This effect was observed in bilateral posterior electrodes. Note that healthy *controls* and patients with *intact* amygdala showed a more positive response to fearful compared to neutral faces, while patients with *lesions* to amygdala showed the opposite- a more negative response for fearful compared to neutral faces. Interestingly, expression effect in this early time window seems to

be affected by the lesion site and not by the response bias. Recall that patients with *intact* amygdala had abnormal fear bias and nevertheless they showed normal early ERP expression effects, while patients with *lesions* to the amygdala who had like-normal fear bias responses showed a different ERP expression response. This may appear to be inconsistent with the results from the healthy *controls* reported above, where the size of the expression effect at P1 predicted subjects' fear bias. To formally test the effect of early ERP expression response on subjects' fear bias, I computed correlations between subjects fear bias and the size of the expression effect.

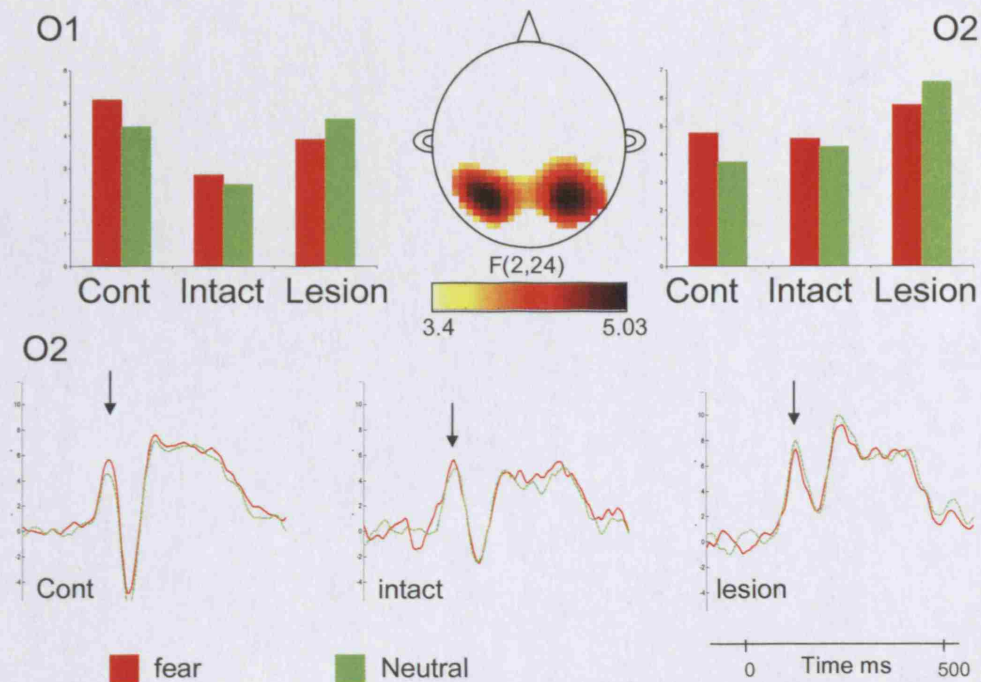


**Figure 9.4 face effect in patient groups**

Differential response for upright faces versus houses was tested separately in each patient group. On the left, SPM t-maps threshold  $P < 0.05$ , for the contrast face < houses for the two early time windows. On the right, time courses plots from electrodes in vicinity to the peak observed in the SPMs. Green dashed line response for upright faces; blue, response for houses.



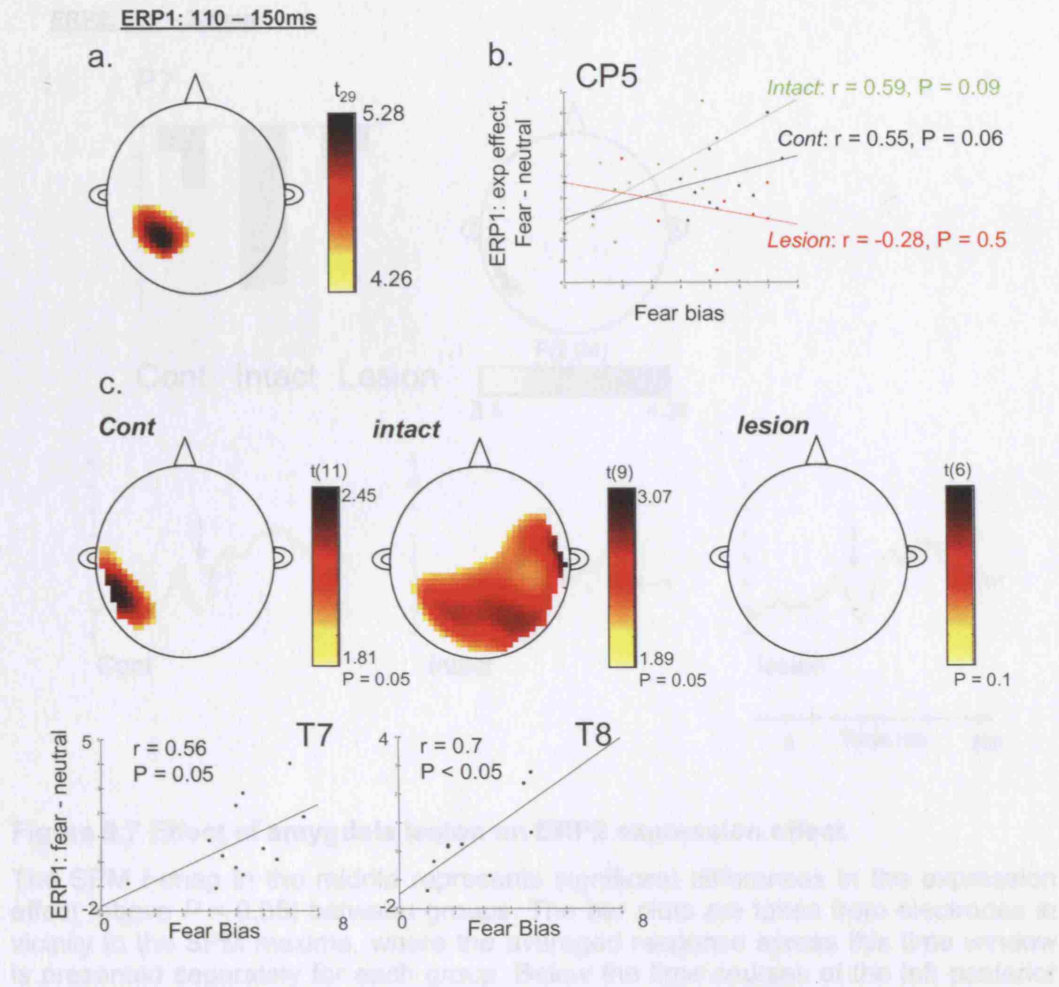
## ERP1: 110 – 150ms



**Figure 9.5 Effect of amygdala lesions on ERP1 expression effect**

The SPM F-map in the middle represents significant differences (above  $P < 0.05$ ) between groups for the expression effect (fearful vs. neutral). The bar plots are taken from electrodes in the vicinity of the SPM maxima, where the averaged response across this time window is presented separately for each group. Below the time course of the right posterior electrode is plotted, with the error pointing to the P1 effect.

Similar to the healthy *controls*, an effect of fear bias over all subjects, independent of group differences, was observed in left posterior electrodes (**Fig. 9.6a**). However, a closer examination revealed that this effect was significant only for the *intact* amygdala group and healthy *controls* but not for the *lesion* group. The result demonstrated that a *lesion* to the amygdala not only reverses the P1 expression effect but also abolishes its influence on subjects' fear bias. In other words intact amygdala was essential for an early differential expression effect and only when the amygdala was intact were early ERPs associated with subjects' fear bias. This result suggests that patients with a *lesion* to the amygdala rely on a different mechanism to interpret fear in expression than healthy *controls* and patients with *intact* amygdala.



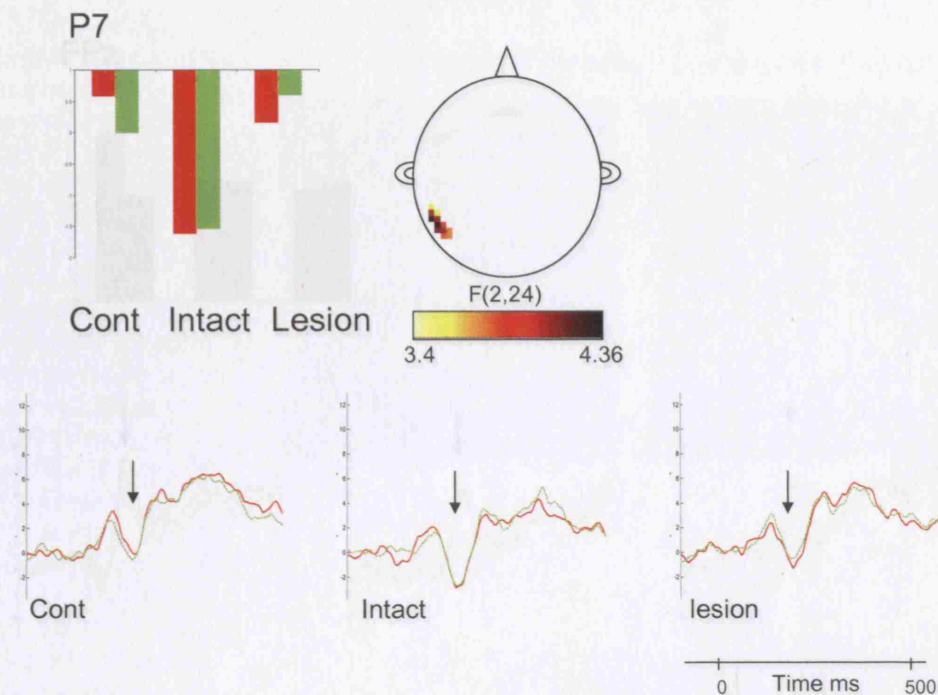
**Figure 9.6: Interaction of fear bias effects and lesion site at ERP1**

**a.** SPM t-map (threshold at  $P < 0.05$ ) depicting significant modulation of the expression effect (fear – neutral) by the covariate: subjects' fear bias across all subjects where group effect is controlled. **b.** Scatters of expression effect and fear bias plotted with a regression line fitted separately for each group. **c.** SPM t-maps depicting significant positive correlation between the size of expression effect and subjects' fear bias, separately for each group, with the correlations plotted below for the *control* and *intact* groups.

At the second time window (155 – 200msec; **Fig. 9.7**) there was still a significant interaction between expression effect and group, though its extent was limited to left lateral electrodes. The pattern of the interaction changed with healthy *controls* maintaining the differential expression effect (i.e. fear > neutral) but this effect was no longer apparent for the *intact* or the *lesion* groups.



## ERP2: 155 – 200ms

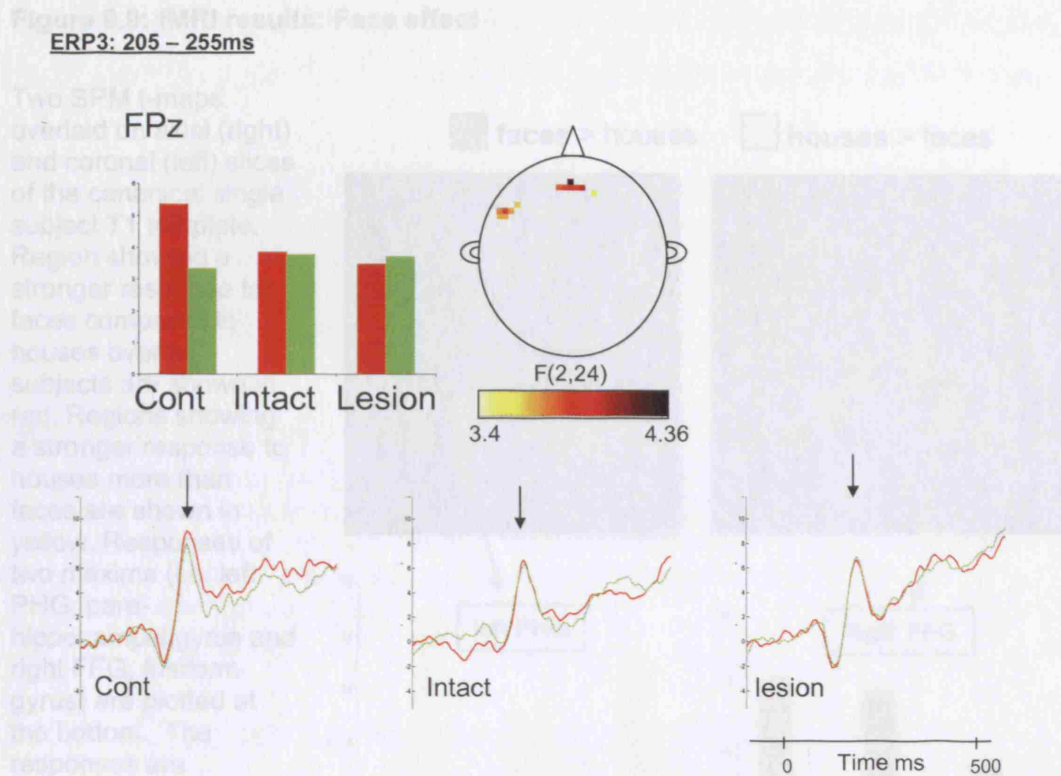


**Figure 9.7 Effect of amygdala lesion on ERP2 expression effect**

The SPM F-map in the middle represents significant differences in the expression effect (above  $P < 0.05$ ) between groups. The bar plots are taken from electrodes in vicinity to the SPM maxima, where the averaged response across this time window is presented separately for each group. Below the time courses of the left posterior electrode are plotted, with the error pointing to the ERP2 time window.

At the second time window, fear bias effects across all subjects independent of group, were evident in the same electrodes ( $P < 0.05$ ). But when inspecting each group on its own, significant modulation of the expression effect by subjects' fear bias was observed only in the healthy *controls* (**Fig. 8.6**) and none were observed in the *intact* and *lesion* amygdala patients.

At the last time window that was investigated here (205 – 250msec) the interaction of group and expression propagated to frontal electrodes. While healthy *controls* maintained the expression effect (fear > neutral), this effect was completely abolished in the *intact* and the *lesion* groups who showed no differential response that related to expression. Subjects' fear bias did not affect the extent of differential expression response at this time window.



**Figure 9.8** Effect of amygdala lesion on ERP3 expression effect

The SPM F-map in the middle represents significant differences in the expression effect (above  $P < 0.05$ ) between groups. The bar plots are taken from electrodes in vicinity to the SPM maxima, where the averaged response across this time window is presented separately for each group. Below the time course of the middle frontal electrode is plotted, with the error pointing to location of ERP3.

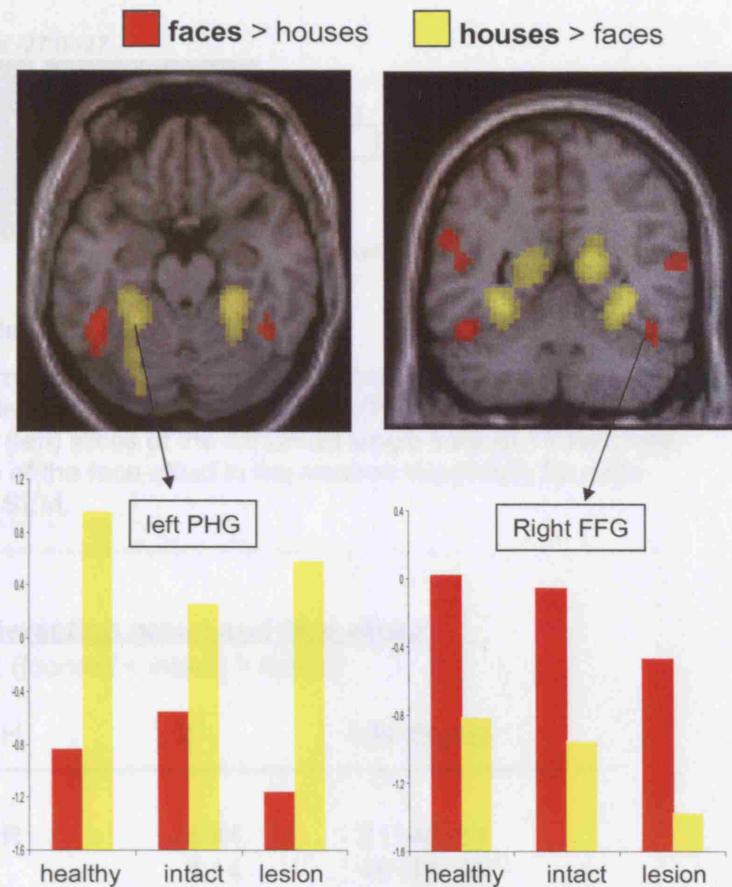
### 9.2.4 fMRI experiment

**Face effect** – A comparison of faces vs. houses was performed across all subjects to establish face selective and house selective responses. As expected robust greater responses for faces compared to houses were evident in bilateral FFG and a larger activation for houses compared to faces were observed medially in bilateral PHG (**Fig. 9.9**). Responses from maxima voxels are plotted separately for each group in **Figure 9.9**. Note that a similar effect size (faces vs. houses) is observed independent of group or lesion location. This demonstrates that the three groups did not differ in temporal-occipital network activation for faces and houses.



**Figure 9.9: fMRI results: Face effect**

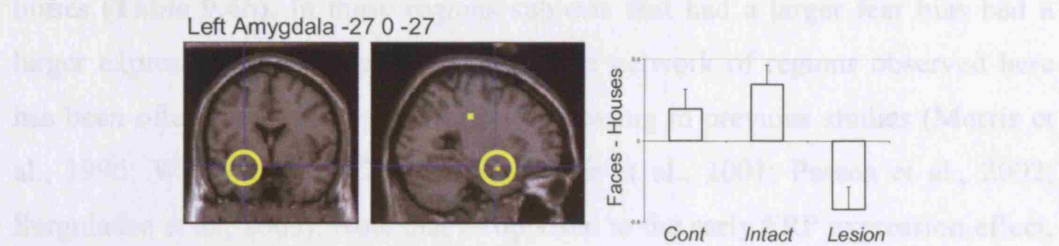
Two SPM t-maps overlaid on axial (right) and coronal (left) slices of the canonical single subject T1 template. Region showing a stronger response to faces compared to houses over all subjects are shown in red. Regions showing a stronger response to houses more than faces are shown in yellow. Responses of two maxima (i.e. left PHG, para-hippocampal gyrus and right FFG, fusiform gyrus) are plotted at the bottom. The responses are presented separately for each group, with red showing the response for faces and yellow the response for houses,



However, a direct comparison between groups revealed a differential response in the left amygdala, with *control* and *intact* patients showing stronger activation to faces than houses, and *lesion* patients showing the opposite (**Fig. 9.10**). This result is not surprising as most patients in the *lesion* group had an abnormal left amygdala (**Table 9.1**). Similar group differences in face effects were observed also in right anterior insula and right IPS (**Table 9.3**).

The differential face effect observed between groups might not seem compatible with the results reported in the EEG experiment above (see **9.2.3**), where lesions to the amygdala did not affect the differential face ERPs effect. However, recall that I only examined two specific brief time windows (110 – 200ms) while time resolution of fMRI is in the order of seconds and therefore represent responses

occurring up to 3 seconds post stimulus presentation. Moreover, it might be that fMRI and EEG signals are sensitive to different aspects of the neuronal response.



**Figure 9.10: Interaction lesion site and face effect**

SPM t-map depicting a stronger face effect for the *control* and *intact* groups compared with the amygdala *lesion* group. The results ( $P < 0.001$ ) are overlaid on coronal (right) and sagittal (left) slices of the canonical single subject T1 template. The plots present the size of the face effect in the maxima separately for each group. The error bars are SEM.

**Table 9.3: Interaction group and face effect**

face > house: ([control + intact] > lesion)

Anatomy	H	Z	MNI (x,y,z)
<b>Parietal</b>			
IPS	R	4.44	21 -48 51
		4.14	48 -36 42
IPS	R	3.54	36 -36 45
<b>Frontal</b>			
Insula	R	3.41	45 30 -3
<b>Subcortical</b>			
Amygdala	L	3.73	-27 0 -15

Abbreviations: H, hemisphere; IPS, intraparietal sulcus; L, left, R, right.

**Expression effects** were tested using an ANCOVA model where responses of each group were modelled separately and fear bias covariates was added to control for possible confounds due to differences in perception (i.e. identical to the model used in the EEG see 9.2.3). I first tested for expression effects across all subjects. Larger responses for fearful expressions compared to neutral expression were observed in posterior occipital regions, pre-frontal cortices and in the pulvinar (Table 9.4a), which were independent of subjects' fear bias. Similar to the results of the *controls* (Table 8.3) subjects' fear bias correlated

with the activation of the right IOG, bilateral FFG (**Fig. 9.11**), STS, post-CS and cingulate gyrus differential expression response correlated with subjects' fear biases (**Table 9.4b**). In these regions subjects that had a larger fear bias had a larger expression effect (fear – neutral). The network of regions observed here has been often reported for expression processing in previous studies (Morris et al., 1996; Winston et al., 2004; Vuilleumier et al., 2001; Pessoa et al., 2002; Surguladze et al., 2003). Note that as opposed to the early ERP expression effect, activation in these regions predicted all subjects' fear bias, including the amygdala *lesion* patients. This suggests that this network can be activated even with limited input from the amygdala.

**Table 9.5: Expression related effects**

a. Expression effect (fear > neutral), RFX t test, df = 28

Anatomy	H	Z	MNI (x,y,z)
Calcarine	R	3.34	21 -57 18
IOG	R	3.25	24 -90 -21
IFS	R	4.11	36 48 9
SFG	L	4.08	-45 24 36
		3.52	-27 45 36
Pulvinar	R	3.96	6 -18 12

b. Main effect of fear bias, RFX t test, df = 26

**Occipital**

Parieto-occ	L	3.25	-21 -57 24
IOG	R	3.04	24 -78 -12
FFG	R	2.64	48 -57 -12
	R	2.85	42 -54 -9
aFFG	L	2.69	-24 -30 -21

**Temporal**

STS	L	2.87	-54 -18 -9
antSTS	R	3.08	57 12 -15

**Frontal**

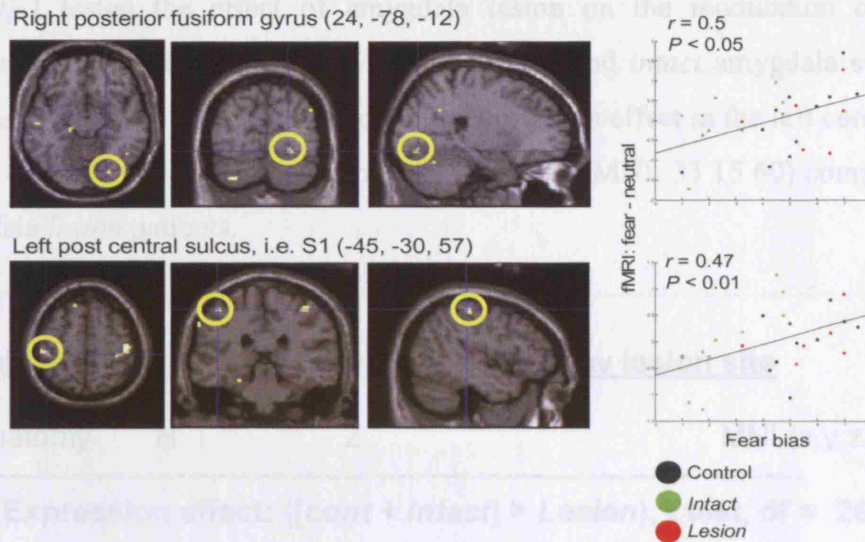
Post CS	R	3.18	48 -24 57
	L	3.20	-45 -30 57
CG	R	3.14	3 54 0

**Subcortical**

PHG	R	2.90	18 -42 0
	L	2.83	-6 30 6

Abbreviations: IOG, inferior frontal gyrus; IFS, inferior frontal sulcus; SFG, superior frontal gyrus; FFG, fusiform gyrus; STS, superior temporal sulcus; CS, central sulcus; CG, cingulate gyrus; PHG, parahippocampal gyrus





**Figure 9.11: fear bias effects across all subjects**

SPM t-map overlaid on the MNI T1 template, depicting positive correlations between expression effect and subjects' fear bias, i.e. the larger the brain response the larger is subjects' fear bias. The scatters on the right represent the response in the maxima of these two regions plotted against subjects fear biased. Note that the statistics test for the correlations in the scatter do not control for group effect and thus have lower values than the ones in the SPM analysis.

**Interaction of expression effect and lesion site** – Effects of amygdala lesions on expression processing independent of perception biases were tested by comparing the amygdala *lesion* to the *intact* amygdala patients and to healthy *controls*. This comparison revealed regions within the frontal cortex: right CG (**Fig. 9.12a**), left OFC and inferior frontal sulcus (**Table 9.5a**) that showed a larger expression effect in patients with *intact* amygdala and healthy *controls* compared to patients with *lesions* to the amygdala. This suggests that these regions receive input from the amygdala, and attenuate their response due to lack of amygdala inputs. The opposite response pattern was observed in the left STG, posterior CG and right inferior frontal gyrus. These regions showed larger responses in patients with amygdala *lesions* compared to healthy *controls* and patients with *intact* amygdala (**Fig. 9.12b**, **Table 9.5b**). Such a pattern might arise due to lack of inhibitory projections from the amygdala. Alternatively these regions might support a compensatory mechanism consequent upon the lack of amygdala responses in processing fear expression.

Finally, I tested the effect of amygdala lesion on the modulation of brain responses by subjects' fear bias. Healthy *control* and *intact* amygdala subjects' fear bias showed stronger correlation with expression effect in the left cerebellum (MNI: -27 -69 -42) and right superior frontal gyrus (MNI: 33 15 60) compared to amygdala *lesion* patients.

**Table 9.5: Interaction - expression effect by lesion site**

Anatomy	H	Z	MNI (x,y,z)
---------	---	---	-------------

**a. Expression effect: ([*cont* + *Intact*] > *Lesion*), t test, df = 26**

**Frontal**

CG	R	3.47	12 42 6
IFS	L	3.46	-27 3 36
OFC	L	3.17	-21 48 -6

**b. Expression effect: (*Lesion* > [*cont* + *Intact*]), t test, df = 26**

**Temporal**

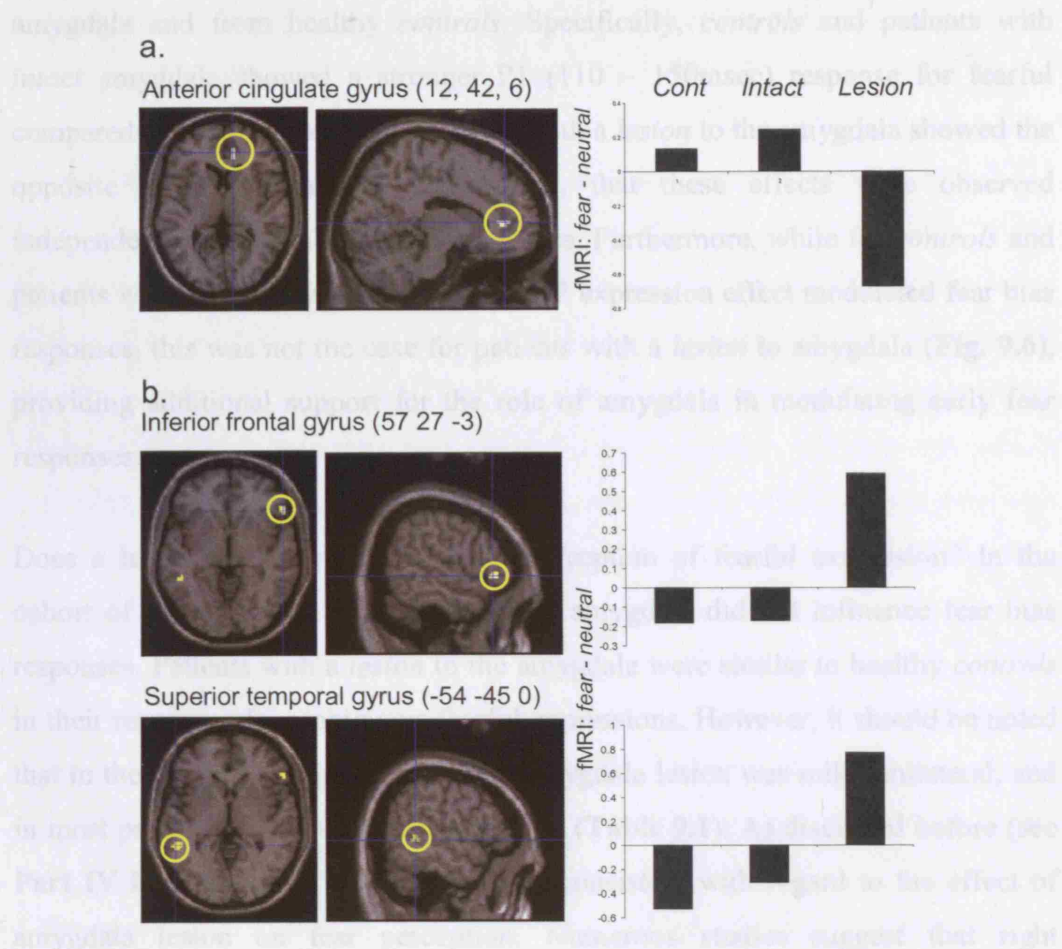
STS	L	3.15	-54 -45 0
	L	3.15	-48 -45 -3

**Frontal**

CG	L	3.77	-12 -51 42
IFG	R	3.73	57 27 -3

Abbreviations: CG, cingulate gyrus; IFS, inferior frontal sulcus; OFC, orbital frontal cortex; STS, superior temporal sulcus; IFG, Inferior frontal gyrus.





**Figure 9.12: Interaction expression effect by lesion site**

SPM t-map overlaid on the MNI T1 template, **a.** depicting larger expression effect for healthy controls and patients with intact amygdala compared to patients with lesion to the amygdala. **b.** Regions that show stronger response for the patient with lesion to the amygdala compared with control and patients with intact amygdala. The plots represent estimated responses for each group at the maxima.

### 9.3 DISCUSSION

The aim of this study was to test the fast route hypothesis for expression processing. This was done by comparing an early ERP differential expression response observed in healthy volunteers (**Chapter 8**) to ERPs obtained from two temporal lobe epileptic patients groups, one with *intact* amygdala and the other with a *lesion* to the amygdala. In addition the effects of the amygdala lesion on fear perception and on distant brain regions using fMRI were tested.

Is there a fast expression processing route mediated via the amygdala? The results observed here suggest that amygdala influences an early differential expression response. Patients with a *lesion* to the amygdala differ from patients with an *intact*

amygdala and from healthy *controls*. Specifically, *controls* and patients with *intact* amygdala showed a stronger P1 (110 – 150msec) response for fearful compared to neutral faces while patients with a *lesion* to the amygdala showed the opposite pattern (**Figs. 9.5, 9.7**). Note, that these effects were observed independent of subjects' fear bias responses. Furthermore, while for *controls* and patients with *intact* amygdala, an early ERP expression effect modulated fear bias responses, this was not the case for patients with a *lesion* to amygdala (**Fig. 9.6**), providing additional support for the role of amygdala in modulating early fear responses.

Does a lesion to the amygdala affect perception of fearful expression? In the cohort of subjects used here an abnormal amygdala did not influence fear bias responses. Patients with a *lesion* to the amygdala were similar to healthy *controls* in their responses for ambiguous fearful expressions. However, it should be noted that in the cohort of patients used here, amygdala lesion was mild, unilateral, and in most patients was in the left hemisphere (**Table 9.1**). As discussed before (see **Part IV Introduction**) the literature is inconsistent with regard to the effect of amygdala lesion on fear perception. Numerous studies suggest that right hemisphere lesions are more associated with impairments in expression perception (Meltti et al., 2003; Anderson et al., 2000; Kucharska-Pietura et al., 2003; Benuzzi et al., 2004) but not all studies showed this (Brierley et al., 2004); others argue that only bilateral amygdala lesions result in expression perception impairments (Adolphs et al., 1995). Thus, the side and extent of the amygdala *lesion* in our patients might explain the lack of perception impairments. However, in contrast to lesion studies, neuroimaging studies often report larger differential expression responses in the left than right amygdala (Morris et al., 1996, 1998; Idaka et al., 2001). One way to resolve this puzzle is to consider a differential role for the left and right amygdala, with left amygdala involved more in automatic processing and the right with conscious perception of expression (though opposite roles for the left and the right amygdala have also been suggested by Morris et al., 1999). The results here are consistent with such a proposition, as most patients here had an abnormal left amygdala and showed like-normal fear perception but an abnormal early brain response for fear stimuli, though a direct comparison

between lesion to right and left amygdala needed to be performed to test this hypothesis formally.

Does a lesion to the amygdala affect expression responses in distant regions? The fMRI results provided complementary information to the EEG and to the behaviour experiments. Differential responses for fearful expression that depended on amygdala lesion were observed in the anterior CG, OFC and IFS where patients with a *lesion* to the amygdala showed weaker expression effect compared to *intact* amygdala patients and healthy *controls*. An opposite pattern was observed in the posterior CG, IFG and left STG where patients with amygdala lesion showed a larger expression effect compared to the other two groups (**Fig. 9.12**).

The result reported here did not replicate the result reported by Vuilleumier et al. (2004). The results diverge especially regarding the differential effect of the amygdala on posterior regions. The current study suggests that lesions to the amygdala influence frontal regions, while posterior-temporal regions (e.g. FFG, STS) were more related to perception when group effects were controlled. In Vuilleumier et al. (2004) an amygdala lesion affected activation in occipital-temporal regions (e.g. FFG, STS) though they also observed effects in anterior CG. One possible way to account for this discrepancy is by considering the effects of fear bias on posterior brain region activation. In the case of their study, subjects' differential fear bias might have confounded the interpretation. Benuzzi et al. (2004) studied medial temporal epileptic (MTLE) patients and showed a similar association between perception and occipital-temporal activation as observed here. They distinguished patients based on lesion side rather than on the structure that is involved (i.e. with or without lesion to amygdala). They show that patients with right MTLE are impaired in fear recognition compared to healthy *controls*, and do not show increased response for fearful compared to neutral expressions in any brain region, while left MTLE had like-normal fear perception and show like-normal increased responses to fearful compared to neutral expressions in occipito-temporal cortices. However left MTLE patients differ from the healthy *controls* in activation of right inferior frontal gyrus and posterior CG as observed here (**Table 9.5**). Unfortunately, a direct comparison between the

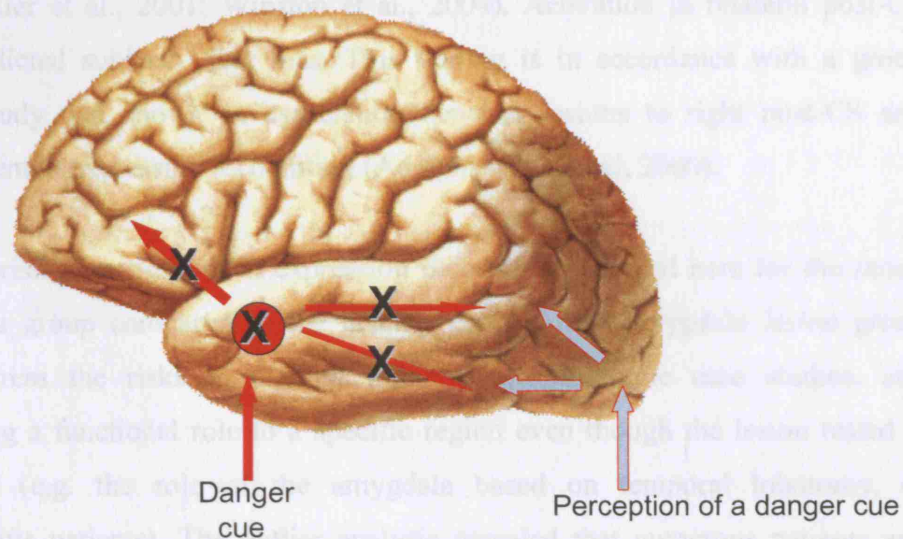
groups was not reported (Benuzzi et al., 2004) therefore it is difficult to estimate the significance of the differences observed.

The effect of projections from the amygdala was also investigated in two fMRI studies that used connectivity analysis. These studies provide contrasting results (Morris et al., 1998; Idaka et al., 2001). Both studies use psychophysiological (PPI) analysis (Friston et al., 1997) testing for left amygdala effects during the conditions of negative vs. happy/neutral expression. While Morris et al. (1998) observed mostly left amygdala effects on occipital-temporal regions (e.g. FFG, IOG, hippocampus), Idaka et al. (2001) observed effects of left amygdala output on left prefrontal cortices during fearful face conditions. Taken together, amygdala response to fearful expression influences both occipital-temporal and prefrontal cortices. Based on the results reported here, I suggest that fearful response in occipito-temporal regions relates more to perception (Rolls et al., 1999) and can be generated even without a signal from the amygdala, while the amygdala directly affects activation in bilateral IFG and anterior CG and it is independent of perception.

What is the role of the amygdala in fear processing? Here, I demonstrated that at the earliest ERP (P1) a significant expression effect was observed consequent upon an amygdala lesion. An abnormal amygdala changed early fear evoked responses and this was observed even though patients show normal fear perception. Moreover, the unique cohort of patients examined here, enabled me to disentangle fear perception from amygdala lesion effects. An early differential ERP response was observed in patients with an *intact* amygdala even though their fear perception was abnormal. These *intact* patients showed similar frontal activation as healthy controls, but differed in their occipito-temporal activation from healthy *controls* and from patients with a *lesion* to the amygdala. This result supports the dual route hypothesis (LeDoux, 1996) whereby amygdala is involved in preparing an organism to respond to a danger situation, as perhaps triggered by fearful expressions i.e. a potential cue for threat, while an explicit recognition of expression relies on other neuronal cortical mechanisms (such as the occipital-temporal route, **Fig. 9.13**). Input from the amygdala in this case might serve as an additional input for these explicit recognition processes that facilitate recognition,

but it is not essential. This view might explain the inconsistent results observed in the lesion literature regarding the role of the amygdala in fear perception (Adolphs et al., 1999). It suggests that maybe the role of the amygdala should be tested using autonomic measures rather than perception.

#### Damaged model.



**Figure 9.13 Model for processing fearful expressions**

A cue for a potential danger situation (such as the view of a scared person) is transmitted rapidly to amygdala (red circle) to enable it to prepare bodily responses. Amygdala with its vast connections with cortical regions then projects to autonomic control centres and to regions that engage in processing the sensory input into perception. Amygdala projections may aid to perception but it is not essential.

Interestingly, only in the case of an intact amygdala, early P1 and superior frontal gyrus activations predicted subjects' fear perception. A recent published case report supports the role of intact amygdala in fear perception (Pegna, et al., 2005). This study shows that in an extreme case, where the occipito-temporal pathway is abolished such as the case of blindsight patients, the amygdala signal increases the ability to correctly guess the expression (Pegna, et al., 2005; Morris et al., 2001). Note that the effect reported by Pegna et al. is small (only 61% correct with chance being 50%, Pegna et al., 2005), thus the amygdala on its own cannot fully accomplish like-normal fear perception, presumably intact processing of occipital-temporal regions are needed for that task.



How do we recognize fear expression? Activation in a network of regions was correlated with subjects' fear bias responses, independent of group effects (Table 10.3). Regions within the occipito-temporal cortex including bilateral FFG, PHG and right STS showed larger expression effects in subjects who had a larger tendency to 'read' fear in an expression. These regions have been previously reported to show differential expression response (Benussi et al., 2004; Vuilleumier et al., 2001; Winston et al., 2004). Activation in bilateral post-CS also predicted subjects' fear bias. This finding is in accordance with a group lesion study that shows an association between lesions to right post-CS and impairment in expression recognition (Adolphs and Tranel, 2000).

The surprising impairment in expression perception observed here for the *intact* amygdala group compared to the healthy *controls* and amygdala *lesion* group might stress the risks in making inferences from single case studies, and attributing a functional role to a specific region even though the lesion tested is extended (e.g. the role of the amygdala based on temporal lobectomy, or encephalitis patients). The outlier analysis revealed that numerous patients and healthy *controls* showed outlier perception of various expressions, with no correlation to a specific brain damage. This suggests that people rely on different strategies in labelling expressions and these should be taken into account when analysing and interpreting results, especially in brain imaging studies. Moreover, not all lesion studies have reported a correlation between amygdala involvement and expression impairments (Rapcsak et al., 2000; Hamman and Adolphs, 1999) suggesting that alternative routes for processing expression might exist that do not involve amygdala, as shown here.

To summarize, in this study I demonstrated that projections from the amygdala influence an early response for fearful expression, supporting a fast route hypothesis. These projections affect subjects' fear bias perception, but only if the amygdala is intact. I also argue that recognizing fear can be achieved with an abnormal amygdala, possibly by compensating for it using frontal and temporal cortices.

# CHAPTER 10:

## GENERAL CONCLUSIONS

---

The aim of this thesis was to test three hypotheses drawn from cognitive and neuroanatomical models of face processing (see **Chapter 1 Introduction**). This chapter will be a brief summary of the findings and conclusions in light of these hypotheses.

### 10.1 HIERARCHICAL STRUCTURE OF FACE PROCESSING

The hierarchical structure of face processing was investigated along two axes: cognitive and neuro-anatomical. A cognitive hierarchical axis was defined on the basis of the Bruce and Young (1986) model, where processing of physical aspects of a face precede processing of identity and ends with extraction of semantic information. Moreover, a face with a given identity may present in multiple physical representations. Thus any face processing mechanism should be able to reduce these multiple physical representations to a single identity representation. Using morphs of famous faces I demonstrated that observers represent both physical and identity aspects of a face (**Part II**). The physical representation of a face followed the continuous nature of the morphed continua (see **Figs. 4.2**) and was independent of identity and prior familiarity with a face. While representation of face identity was revealed by a tendency to categorize a morph continuum into two discrete identities (see **Figs. 4.1, 4.3, 4.4**). Furthermore, representation of identity was dependent on subjects' prior familiarity with a face (see **Fig. 5.4**). Evidences for physical and identity representations were also observed in two priming experiments. Here,



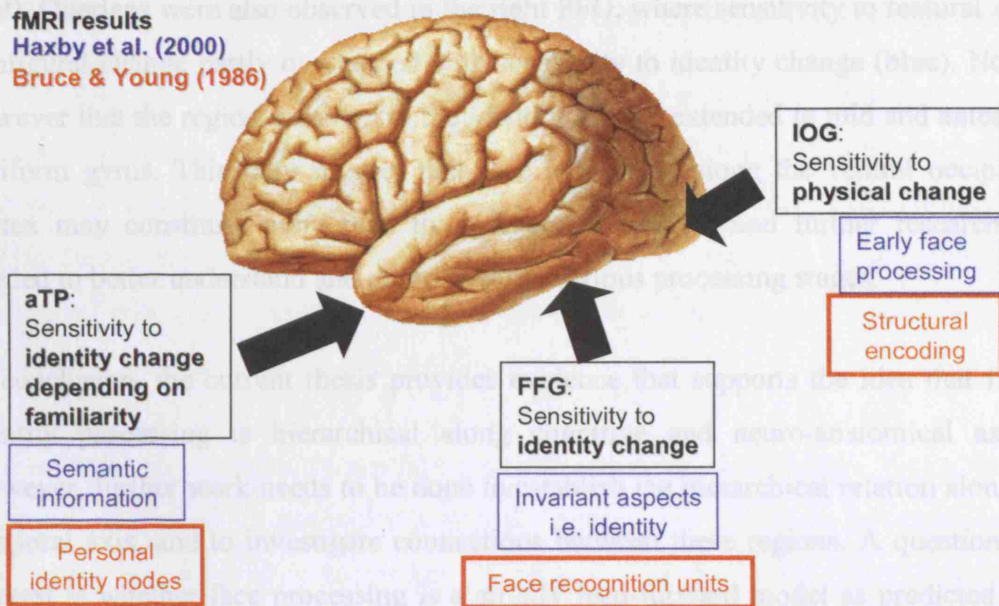
## Chapter 10: General Conclusions

responses were facilitated if a prime and a target shared the same physical properties and an additional facilitation occurred if both had the same perceived identity (see Figs. 5.2 and 5.3).

Interestingly the relative contribution of physical and identity processing to behavioural responses depended on task. Physical processing was more pronounced during the similarity judgement task than the identity classification task; while identity processing was more pronounced in the identity classification than in the similarity task (compare Figs. 4.2 to 4.3). Identity processing was also more pronounced than physical processing in the familiarity judgement task (Fig. 5.2).

In accordance with the cognitive axis, hierarchical structure was observed along a neuroanatomical axis (Fig. 10.1). In which posterior occipital cortices (i.e. IOG) showed greater sensitivity to physical aspects of faces, the right FFG showed greater sensitivity to the face identities and bi-lateral anterior temporal pole cortices showed sensitivity to face identities that depended on the familiarity of a face. These findings accord with predictions of previous neuroanatomical models (de Renzi et al., 1991; Haxby et al., 2001).

Previous researchers (Kanwisher et al., 1997; Haxby et al., 2000) have attributed the FFG processing into different cognitive processing stages. Kanwisher et al., (1997) argue that the FFG process the structural code of a face, while Haxby et al., (2000) hypothesis that FFG stores face recognition units (FRUs). Here, I would suggest that the separation of structural codes and FRUs to two different processing stages (Bruce and Young, 1986) may be redundant. Thus a single neural representation can encode face identity and signal whether an identity is of a familiar face (e.g. by reducing the response to a familiar face). Note, that such a mechanism also does not predict different recognition processes for familiar and unfamiliar faces as opposed to what was proposed by Bruce and Young (1986).



**Figure 10.1: Hierarchical neuro-anatomical model for face processing**

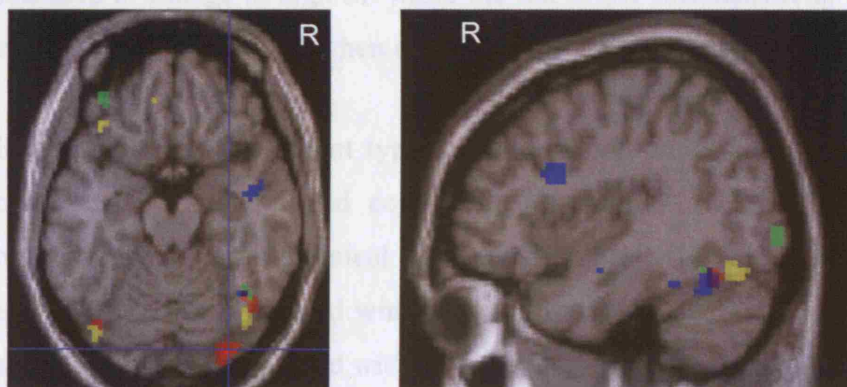
A proposed hierarchical model for face processing is presented along a lateral view of a cartoon brain, with the results of the imaging experiment (**Chapter 5.1**) in black, neuro-anatomical prediction from the Haxby et al., (2000) model in blue, and the homologue cognitive axis based on the Bruce and Young model (1986) in orange.

The spatial frequency (SF) experiment (**Chapter 6**) also provided evidence that support a neuro-anatomical hierarchical structure for processing faces. Here, a functional dissociation was observed in posterior occipital regions, with the right IOG processing high SF and MOG processing low SF information from a face. An anterior region within the right FFG may provide a point of convergence of these two types of information. Similarly featural and 2<sup>nd</sup>-conf processing (**Chapter 7**) were dissociated in posterior occipital cortices, with the right LOS processing featural information while the left MOG and bi-lateral IOG processing 2<sup>nd</sup>-conf information, while the right FFG was sensitive to both features and 2<sup>nd</sup>.conf information of a face.

In order to better describe the relation between the physical and identity processing identified by the morphing experiment and processing of feature configuration the results of these studies were overlaid on the same brain (**Figure 10.2**). As can be seen the functional dissociation between featural (green) and configural (red) processing in the right IOG was more posterior than the sensitivity observed to the overall change in the physical appearance of a face (yellow). However, in the left IOG sensitivity to physical change (yellow) overlapped sensitivity to 2<sup>nd</sup>.conf change

(red). Overlaps were also observed in the right FFG, where sensitivity to featural and configural change partly overlapped with sensitivity to identity change (blue). Note, however that the region sensitive to the identity change extended to mid and anterior fusiform gyrus. This may suggest that face processing along the ventral occipital cortex may constitute more than three stages (**Fig 10.1**) and further research is needed to better understand and describe these various processing stages.

In conclusion, the current thesis provides evidence that supports the idea that face identity processing is hierarchical along cognitive and neuro-anatomical axes. However, further work needs to be done to establish the hierarchical relation along a temporal axis, and to investigate connections between these regions. A question of interest is whether face processing is a strictly feed-forward model as predicted by Bruce and Young (1986) or is more complex including feedback and lateral connections.



Feature-configuration experiment (Chapter 8)

Sensitivity to 2<sup>nd</sup> order configural change (dependent on subjects variability)

Sensitivity to featural change

Morphing experiment (Chapter 6)

Sensitivity to change in physical aspect of a face

Sensitivity to change in perceived identity

**Figure 11.2: Neural correlates of features, 2<sup>nd</sup>-conf, physical and identity processing in faces**

Results from the feature-configuration and morphing experiments are overlaid on the same sagittal and axial slices for comparison, using different color coding (see index above). For presentation the SPM maps are threshold at 0.005 uncorrected.

## 10.2 WHAT CONSTITUTES EARLY FACE PROCESSING?

Two assumptions guided the investigation of early face processing. Based on neuro-anatomical models I postulated that early face processing are implemented in posterior occipital cortices and that in early stages of face processing different types of information are processed separately. In other words, I predicted that a functional-anatomical dissociation would be evident in posterior occipital cortices. The results presented in **Part III** confirm this prediction.

Decomposing information from a face into different types was realized in two ways. The first was based on neurophysiological findings that relates to the way visual information is conveyed to the cortex. Namely via the parvo-cellular pathway and magno-cellular pathway that convey high and low SF information, respectively (De Valois and De Valois, 1990). Using hybrid stimuli that were composed of different high and low SF filtered faces I demonstrated that sensitivity the right IOG was sensitive to change in high SF while the left MOG was sensitivity to low SF change and increased its respond when attending low SF faces (**Fig. 6.2, Chapter 6**).

In a second study, different types of information were defined based on cognitive constructs i.e. featural and configural (**Chapter 7**). Similar to the SF study, I observed functional-anatomical dissociation in posterior occipital regions. Activation in bi-lateral LOS correlated with featural processing and activation in the left MOG and bilateral IOG correlated with 2<sup>nd</sup> order configural processing (**Figs. 7.5 and 7.6**).

Taken together, these results support the hypothesis that link processing of SF information to processing of the cognitive constructs of a face (Farah et al., 1997; **Fig. 7.11**). In light of this hypothesis the right LOS engages in processing high SF information and therefore shows a greater sensitivity to change in facial features; the left MOG is involved in processing low SF information and showed greater sensitivity to change in a 2<sup>nd</sup>.conf of a face. However, note that not all the results reported here support such a simplistic hypothesis between SF, feature and configural processing; for example the right MOG showed greater sensitivity to low SF information and also sensitivity to change in features. Thus, further experimental



work needs to be done to clarify the potential relations between SF processing and the associated cognitive constructs.

Interestingly, I observed that the quality of early coding of information in a face in the posterior visual cortices influences later recognition of face identity. Specifically, subjects that coded 2<sup>nd</sup> order configural information of a face by recruiting bi-lateral IOG, were better in recognizing faces.

In conclusion, I suggest that early face processing constitutes of multiple processes. In these processes different types of information from a face are coded using separate neuronal networks within posterior occipital cortices. Specifically, the separation of SF information in a viewed face that starts at the eye is maintained throughout early stages of face processing and this information converges only in more anterior regions of a face processing hierarchy, such as the FFG. Similarly, coding of featural and configural information is performed in dissociated anatomical structures. However, recall that “early” was defined here along cognitive and neuro-anatomical axes, and it remains unclear whether these functional dissociations also appear along a temporal axis. Furthermore, without connectivity analysis I cannot conclude that the output of the various posterior occipital regions is fed forward to the more anterior occipital regions. This leaves several questions open: the first is there hierarchy relations between the different types of face information within posterior occipital cortices, as would be predicted by the coarse-to-fine (Buillier et al., 2001; Lamme et al., 2001) and global-to-local hypotheses (Farah et al., 1997). Second does the different processing stream in posterior occipital cortex converge in the right FFG, or alternatively processing in the right FFG and posterior occipital cortices have different roles and operate in parallel; for example may detect face while another encode identity (de Gelder and Rouw, 2001).

### 10.3 EARLY PROCESSING OF FACIAL EXPRESSION

The final hypothesis that was addressed in this thesis relates to processing of facial expression. Bruce and Young (1986) and Haxby et al. (2000) proposed a parallel route for processing expressions. Both predict that this route diverges from the identity route after an initial processing of visual information from a face (**Figs. 1.1**

and 1.2). However, a recent study demonstrated that even in the absence of visual processing recognition of expression can still be established and the authors argue that this recognition is mediated via the amygdala (Pegna, et al., 2005). Furthermore it has been proposed that the amygdala mediates a fast route for expression processing that bypass visual cortex (Vuilleumier et al., 2003, 2004).

I tested the fast route hypothesis along temporal and neuro-anatomical axes using EEG and fMRI. In healthy volunteers I observed differential sensitivity to faces compared to houses in bilateral posterior electrodes at P1 (110-150ms, **Fig. 8.4**). In the same time window there was also a differential response to facial expressions (**Fig. 8.5**). Furthermore, the size of the P1 expression effect predicted subjects' fear perception. In terms of the neuro-anatomical axis, differential effects of faces compared to houses were observed in posterior occipital regions (i.e. the calcarine sulcus, right IOG, left MOG, FFG) and in left amygdala. Differential effects of expressions were observed in posterior occipital regions (i.e. the Calcarine, IOG, FFG) and in temporal regions (STS, hippocampus) amongst other. However, due to lack of temporal resolution in fMRI, one cannot conclude which of these regions have contributed to the early ERP effects.

There are two ways to account for results from the healthy volunteers: one, information concerning facial expression is already extracted in the very early stages of visual face processing (as would be suggested by fMRI results, i.e. differential response in posterior occipital cortices for expression), the second is that there is a parallel route that bypasses the visual cortex for expression processing. To distinguish between these two alternative explanations I conducted a second experiment with temporal lobe epileptic patients that either had a lesion or an intact amygdala. The rationale was that if there is a parallel route for expression processing and the amygdala plays a crucial role in it, an abnormal amygdala will affect brain responses for expression processing but will not affect early visual processing of a face. Indeed I observed that lesions to the amygdala did not affect early visual face processing (comparing responses to faces versus houses) i.e. P1 and N170 (**Fig. 9.3b**) but had a dramatic effect on early expression processing P1 and ERP2 (**Fig. 9.4**). The fMRI showed that differential expression effects were observed in posterior occipital cortices (i.e. calcarine, right IOG) independent of amygdala lesions (**Table**

**9.4**), while activation in the frontal and prefrontal regions were affected by amygdala lesions (**Fig. 9.12, Table 9.5**).

The results reported here do not support the prediction that expression processing are executed only after an initial processing of visual information from a face (Bruce and Young, 1986; Haxby et al., 2000). One way to reconcile this contradiction is to consider two routes for expression processing, one which is mediated via the amygdala and a second mediated via the visual cortex (LeDoux, 1996; Critchely et al., 2000; Phillips et al., 2004). Here, patients with a *lesion* to the amygdala showed an abnormal early ERP expression effect but showed normal recognition of fearful expressions. In contrast, patients with an *intact* amygdala showed normal ERP expression effects but showed an abnormal recognition of fearful expressions. Furthermore, activation in the occipito-temporal cortices including the IOG, STS and FFG positively correlated with subjects fear perception and not with an abnormal amygdala. In contrast activations in prefrontal regions were affected by amygdala lesion and not by fear perception. This dissociation supports a dual route hypothesis for visual emotion processing (LeDoux, 1996). Thus, occipito-temporal cortices are involved in recognizing expression in faces, while an amygdala-prefrontal route generates a warning signal that alerts an organism to potential danger. In case of an intact amygdala these two pathways interact and influence each other. Further research involving neuropsychological patients and imaging needs be done to further establish the existence of these two expression processing routes.



## **List of figures**

Figure 1.1	Bruce and Young (1986) Face Recognition Model.....	16
Figure 1.2	Haxby et al., (2003) Distributed neural network for face perception.....	19
Figure 1.3	Hierarchical face processing.....	29
Figure 1.4	Familiar and unfamiliar face recognition.....	32
Figure 1.5	Face processing of identity and non-identity information.....	35
Figure 1.6	Face selective cells in Monkey's brain.....	36
Figure 2.1	The spin of a proton.....	55
Figure 2.2	Proton precession.....	56
Figure 2.3	T1 weighted image.....	58
Figure 2.4	T1 spin echo.....	61
Figure 2.5	Slice select gradient.....	63
Figure 2.6	Magnetic gradients applied to encode spatial information .....	65
Figure 2.7	Echo planner imaging sequence.....	67
Figure 2.8	First level design matrix.....	82
Figure 3.1	Electrical currents in the cortex.....	90
Figure 3.2	The “10-20” montage.....	94
Figure 4.1	Identity classification task.....	107
Figure 4.2	Similarity Judgment task.....	110
Figure 4.3	Identity discrimination task.....	113
Figure 4.4	Perceptual discrimination task.....	116
Figure 5.1	fMRI results: Identity & physical change effects.....	124

Figure 5.2	Gender priming experiment.....	128
Figure 5.3	Familiarity priming experiment.....	131
Figure 5.4	Effects of familiarity on perception.....	133
Figure 5.5	Effect of pre-experimental familiarity – fMRI.....	135
Figure 6.1	Stimuli & experimental design – spatial frequency experiment.....	147
Figure 6.2	fMRI results: Spatial frequency specific effects.....	154
Figure 6.3	fMRI results: Overview of SF effects.....	156
Figure 7.1	Experimental design: Identity discrimination experiment.....	169
Figure 7.2	Identity discrimination – results.....	170
Figure 7.3	Dissociated and associated face processes.....	172
Figure 7.4	fMRI results: Violation of 1 <sup>st</sup> -conf.....	175
Figure 7.5	fMRI results: Features change effects.....	177
Figure 7.6	fMRI results: 2 <sup>nd</sup> -conf change effects.....	178
Figure 7.7	fMRI results: correlation behaviour and fMRI.....	180
Figure 7.8	fMRI results: overview of featural and 2 <sup>nd</sup> -conf effects.....	181
Figure 7.9	Experimental design: Objective measure of face recognition skills.....	184
Figure 7.10	Correlation with subjective rating of face recognition.....	186
Figure 7.11	Early face processes in posterior occipital cortices.....	189
Figure 8.1	Stimuli, hexogen expression task.....	195
Figure 8.2	Expression response bias.....	199
Figure 8.3	One back task, imaging experiments – behaviour results.....	200
Figure 8.4	EEG results: Face effects.....	201
Figure 8.5	EEG results: Expression effects.....	202

Figure 8.6	EEG results: Fear bias effects.....	203
Figure 8.7	fMRI results: Face effects.....	204
Figure 8.8	fMRI results: Fear bias effects.....	207
Figure 9.1	Hexogen expression test – response pattern.....	214
Figure 9.2	Outlier behaviour.....	217
Figure 9.3	One-back task.....	220
Figure 9.4	Face effect in patient groups.....	222
Figure 9.5	Effect of amygdala lesions on ERP1 expression effect.....	223
Figure 9.6	Interaction of fear bias and lesion site at ERP1.....	224
Figure 9.7	Effect of lesion site on ERP2 expression effect.....	225
Figure 9.8	Effect of lesion site on ERP3 expression effect.....	226
Figure 9.9	fMRI results: face effects.....	227
Figure 9.10	fMRI results: interaction lesion site and face effects.....	228
Figure 9.11	fMRI results: fear bias effect across all subjects.....	230
Figure 9.12	fMRI results: Interaction expression effect and amygdala lesion...	232
Figure 9.13	Model for processing fearful expressions.....	236
Figure 10.1	Hierarchical neuro-anatomical model for face processing.....	240
Figure 10.2	Neural correlates of features, 2 <sup>nd</sup> -conf, physical and identity processing in faces.....	241

## **List of tables**

Table 5.1	fMRI results: Identity & physical change effects.....	123
Table 5.2	fMRI results: Pre experimental familiarity effects.....	135
Table 6.1	fMRI results: High spatial frequency effects.....	151
Table 6.2	fMRI results: Low spatial frequency effects.....	152
Table 6.3	fMRI results: High & Low spatial frequency effects.....	155
Table 7.1	fMRI results: 1 <sup>st</sup> -conf effects.....	175
Table 7.2	fMRI results: feature change effects.....	177
Table 7.3	fMRI results: 2 <sup>nd</sup> -conf change effects.....	178
Table 7.4	fMRI results: Correlation fMRI and behaviour.....	180
Table 7.5	Correlation matrix of behaviour experiments.....	187
Table 8.1	fMRI results: Face effects.....	205
Table 8.2	fMRI results: Expression effects.....	206
Table 8.3	fMRI results: Fear bias and expression effect.....	206
Table 9.1	Patients details.....	212
Table 9.2	Outlier analysis – hexogen expression task.....	218
Table 9.3	fMRI results: Interaction group and face effect.....	228
Table 9.4	fMRI results: Expression effects across all subjects.....	232
Table 9.5	fMRI results: Interaction expression effect by lesion site.....	229

## **References**

- Adolphs,R., Tranel,D., Damasio,H., and Damasio,A. (1994). Impaired recognition of emotion in facial expressions following bilateral damage to the human amygdala. *Nature* 372, 669-672.
- Adolphs,R., Tranel,D., Damasio,H., and Damasio,A.R. (1995). Fear and the human amygdala. *J.Neurosci.* 15, 5879-5891.
- Adolphs,R., Damasio,H., Tranel,D., and Damasio,A.R. (1996). Cortical systems for the recognition of emotion in facial expressions. *J.Neurosci.* 16, 7678-7687.
- Adolphs,R., Tranel,D., Hamann,S., Young,A.W., Calder,A.J., Phelps,E.A., Anderson,A., Lee,G.P., and Damasio,A.R. (1999). Recognition of facial emotion in nine individuals with bilateral amygdala damage. *Neuropsychologia* 37, 1111-1117.
- Adolphs,R., Damasio,H., Tranel,D., Cooper,G., and Damasio,A.R. (2000). A role for somatosensory cortices in the visual recognition of emotion as revealed by three-dimensional lesion mapping. *J.Neurosci.* 20, 2683-2690.
- Adolphs,R., Tranel,D., and Damasio,H. (2001). Emotion recognition from faces and prosody following temporal lobectomy. *Neuropsychology*. 15, 396-404.
- Adolphs,R., Tranel,D., and Damasio,A.R. (2003). Dissociable neural systems for recognizing emotions. *Brain Cogn* 52, 61-69.
- Adolphs,R. and Tranel,D. (2004). Impaired judgments of sadness but not happiness following bilateral amygdala damage. *J.Cogn Neurosci.* 16, 453-462.
- Adrian,E.D. and Matthews,B.H. (1934). The Berger rhythm: potential changes from the occipital lobes in man. *Brain* 57, 355-385.
- Allison,T., Ginter,H., McCarthy,G., Nobre,A.C., Puce,A., Luby,M., and Spencer,D.D. (1994). Face recognition in human extrastriate cortex. *J.Neurophysiol.* 71, 821-825.
- Allison,T., Puce,A., Spencer,D.D., and McCarthy,G. (1999). Electrophysiological studies of human face perception. I: Potential generated in occipitotemporal cortex by face and non-face stimuli. *Cerebral Cortex* 9, 415-430.
- Amunts,K., Schleicher,A., Burgel,U., Mohlberg,H., Uylings,H.B., and Zilles,K. (1999). Broca's region revisited: cytoarchitecture and intersubject variability. *J.Comp Neurol.* 412, 319-341.
- Anderson,A.K. and Phelps,E.A. (2000). Expression without recognition: contributions of the human amygdala to emotional communication. *Psychological Science* 11, 106-111.
- Anderson,A.K., Spencer,D.D., Fulbright,R.K., and Phelps,E.A. (2000). Contribution of the anteromedial temporal lobes to the evaluation of facial emotion. *Neuropsychology* 14, 526-536.
- Anderson,A.K. and Phelps,E.A. (2000). Perceiving emotion: There's more than meets the eye. *Curr.Biol.* 10, R551-R554.
- Anderson,A.K. and Phelps,E.A. (2001). Lesions of the human amygdala impair enhanced perception of emotionally salient events. *Nature* 411, 305-309.

- Anderson, A.K. and Phelps, E.A. (2002). Is the human amygdala critical for the subjective experience of emotion? Evidence of intact dispositional affect in patients with amygdala lesions. *J. Cogn Neurosci.* 14, 709-720.
- Anderson, D.N. (1988). The delusion of inanimate doubles. Implications for understanding the Capgras phenomenon. *Br. J. Psychiatry* 153, 694-699.
- Andersson, J.L., Hutton, C., Ashburner, J., Turner, R., and Friston, K.J. (2001). Modeling geometric deformations in EPI time series. *Neuroimage* 13, 903-919.
- Andreasen, N.C., O'Leary, D.S., Arndt, S., Cizadlo, T., Hurtig, R., Rezai, K., Watkins, G.L., Ponto, L.B., and Hichwa, R.D. (1996). Neural substrates of facial recognition. *J. Neuropsychiatry Clin. Neurosci.* 8, 139-146.
- Araque, A., Parpura, V., Sanzgiri, R.P., and Haydon, P.G. (1999). Tripartite synapses: glia, the unacknowledged partner. *Trends Neurosci* 22, 208-215.
- Ashburner, J. and Friston, K.J. (1999). Nonlinear spatial normalization using basis function. *Human Brain Mapping* 7, 254-266.
- Ashburner, J. and Friston, K.J. (2003). Rigid body transformation. In *Human Brain Function*, R. S. Frackowiak, K. J. Friston, C. Frith, R. J. Dolan, C. Price, S. Zeki, J. Ashburner, and W. Penny, eds. Academic Press).
- Ashburner, J. and Friston, K.J. (2003). Spatial normalization using basis functions. In *Human Brain Function*, R. S. Frackowiak, K. J. Friston, C. Frith, R. J. Dolan, C. Price, S. Zeki, J. Ashburner, and W. Penny, eds. Academic Press).
- Ashley, V., Vuilleumier, P., and Swick, D. (2004). Time course and specificity of event-related potentials to emotional expressions. *Neuroreport* 15, 211-216.
- Badcock, J.C., Whitworth, F.A., Badcock, D.R., and Lovegrove, W.J. (1990). Low-frequency filtering and the processing of local-global stimuli. *Perception* 19, 617-629.
- Bar, M. (2003). A cortical mechanism for triggering top down facilitation in visual object recognition. *Journal of Cognitive Neuroscience* 15, 600-609.
- Barton, J.J.S., Cherkasova, M., and O'Connor, M. (2001). Covert recognition in acquired and developmental prosopagnosia. *Neurology* 57, 1161-1168.
- Barton, J.J.S., Press, D.Z., Keenan, J.P., and O'Connor, M. (2002). Lesions of the fusiform face area impair perception of facial configuration in prosopagnosia. *Neurology* 58, 71-78.
- Barton, J.J.S., Cherkasova, M.V., Press, D.Z., Intriligator, J.M., and O'Connor, M. (2003). Developmental prosopagnosia: a study of three patients. *Brain Cogn* 51, 12-30.
- Barton, J.J.S. and Cherkasova, M. (2003). Face imagery and its relation to perception and covert recognition in prosopagnosia. *Neurology* 61, 220-225.
- Barton, J.J.S. (2003). Disorders of face perception and recognition. *Neurol. Clin.* 21, 521-548.
- Barton, J.J.S., Zhao, J., and Keenan, J.P. (2003). Perception of global facial geometry in the inversion effect and prosopagnosia. *Neuropsychologia* 41, 1703-1711.

- Birn, R.M., Saad, Z., and Bandettini, P.A. (2001). Spatial heterogeneity of the nonlinear dynamics in the fMRI response. *Neuroimage* 14, 817-826.
- Blackmore, C. and Campbell, F.W. On the existence of neurons in the human visual system selectivity sensitive to orientation and size of retinal images. *Journal of Physiology* 203, 237-260. 1969.  
Ref Type: Journal (Full)
- Blanc-Garin, J. (1986). Faces and non-faces in prosopagnosic's patients. In *Aspects of face processing*, H. D. Ellis, M. A. Jeeves FRSE, F. Newcombe, and A. Young, eds. (Dordrecht / Boston / Lancaster: Martinus Nijhoff Publishers), pp. 273-278.
- Bobes, M.A., Lopera, F., Garcia, M., Diaz-Comas, L., Galan, L., and Valdes-Sosa, M. (2003). Covert matching of unfamiliar faces in a case of prosopagnosia: an ERP study. *Cortex* 39, 41-56.
- Bodamer, J. (1947). Die prosop-agnosia. *Arch.Psychiatr.Nervenkr.* 179, 6-54.
- Bodamer, J. (1947). Die Prosp-agnosia. *Archive fur Psychiatrie und Zeitschrift fur Neurologie [Archeive of Psychiatry and Journal of Neurology]* 179, 6-53.
- Bornstein, B., Sroka, H., and Munitz, H. (1969). Prosopagnosia with animal face agnosia. *Cortex* 5, 164-169.
- Botzel, K. and Grusser, O.J. (1989). Electric brain potentials evoked by pictures of faces and non-faces: a search for "face-specific" EEG-potentials. *Exp.Brain Res.* 77, 349-360.
- Boutet, I., Collin, C., and Faubert, J. (2003). Configural face encoding and spatial frequency information. *Percept.Psychophys.* 65, 1078-1093.
- Boutsen, L. and Humphreys, G.W. (2002). Face context interferes with local part processing in a prosopagnosic patient. *Neuropsychologia* 40, 2305-2313.
- Boyton, G.M., Engel, S.A., Glover, G.H., and Heeger, D.J. (1996). Linear systems analysis of functional magnetic resonance imaging in human V1. *J.Neurosci.* 16, 4207-4221.
- Breiter, H.C., Etcoff, N.L., Whalen, P.J., Kennedy, W.A., Rauch, S.L., Buckner, R.L., Strauss, M.M., Hyman, S.E., and Rosen, B.R. (1996). Response and habituation of the human amygdala during visual processing of facial expression. *Neuron* 17, 875-887.
- Brennen, T. and Bruce, V. (1991). Context effects in the processing of familiar faces. *Psychol.Res.* 53, 296-304.
- Brett, M., Penny, W., and Kiebel, S. (2003). Introduction to random field theory. In *Human Brain Function*, R. S. Frackowiak, K. J. Friston, C. Frith, R. J. Dolan, C. Price, S. Zeki, J. Ashburner, and W. Penny, eds. (London: Academic Press).
- Brierley, B., Medford, N., Shaw, P., and David, A.S. (2004). Emotional memory and perception in temporal lobectomy patients with amygdala damage. *Journal of Neurol Neurosurgery Psychiatry* 75, 593-599.
- Broks, P., Young, A.W., Maratos, E.J., Coffey, P.J., Calder, A.J., Isaac, C.L., Mayes, A.R., Hodges, J.R., Montaldi, D., Cezayirli, E., Roberts, N., and Hadley, D. (1998). Face processing impairments after encephalitis: amygdala damage and recognition of fear. *Neuropsychologia* 36, 59-70.
- Brown, M.W. and Xiang, J.Z. (1998). Recognition memory: neuronal substrates of the judgement of prior occurrence. *Prog.Neurobiol.* 55, 149-189.



- Bruce, V. and Valentine, T. (1985). Identity priming in the recognition of familiar faces. *British Journal of Psychology* 76 ( Pt 3), 373-383.
- Bruce, V. and Young, A. (1986). Understanding face recognition. *British Journal of Psychology* 77, 305-327.
- Bruce, V., Doyle, T., Dench, N., and Burton, M. (1991). Remembering facial configurations. *Cognition* 38, 109-144.
- Bruce, V., Burton, A.M., and Craw, I. (1992). Modelling face recognition. *Philos. Trans. R. Soc. Lond B Biol. Sci.* 335, 121-127.
- Bruyer, R. (1991). Covert face recognition in prosopagnosia: a review. *Brain Cogn* 15, 223-235.
- Bullier, J. (2001). Integrated model of visual processing. *Brain Res. Brain Res. Rev.* 36, 96-107.
- Bullier, J., Hupe, J.M., James, A.C., and Girard, P. (2001). The role of feedback connections in shaping the responses of visual cortical neurons. *Prog. Brain Res.* 134, 193-204.
- Bulthoff, I. and Newell, F.N. (2004). Categorical perception of sex in familiar but not unfamiliar faces. *Visual Cognition* 11, 823-855.
- Burton, A.M., Bruce, V., and Johnston, R.A. (1990). Understanding face recognition with an interactive activation model. *British Journal of Psychology* 81 ( Pt 3), 361-380.
- Burton, A.M., Young, A.W., Bruce, V., Johnston, R.A., and Ellis, A.W. (1991). Understanding covert recognition. *Cognition* 39, 129-166.
- Burton, A.M., Miller, P., Bruce, V., Hancock, P.J., and Henderson, Z. (2001). Human and automatic face recognition: a comparison across image formats. *Vision Research* 41, 3185-3195.
- Burton, G.J., Haig, N.D., and Moorhead, I.R. (1986). A self-similar stack model for human and machine vision. *Biol. Cybern.* 53, 397-403.
- Burton, L.A. and Labar, D. (1999). Emotional status after right vs. left temporal lobectomy. *Seizure*. 8, 116-119.
- Burton, L.A., Gilliam, D., Flynn, S., Labar, D., and Conn, J. (2002). Global affective memory for faces in patients with temporal lobe epilepsy. *Appl. Neuropsychol.* 9, 234-239.
- Burton, L.A., Wyatt, G., Rabin, L., Frohlich, J., Vardy, S.B., Dimitri, D., and Douglas, L. (2003). Perception and priming of affective faces in temporal lobectomy patients. *J. Clin. Exp. Neuropsychol.* 25, 348-360.
- Buxbaum, L.J., Glosser, G., and Coslett, H.B. (1999). Impaired face and word recognition without object agnosia. *Neuropsychologia* 37, 41-50.
- Buxton, R.B. and Frank, L.R. (1997). A model for coupling between cerebral blood flow and oxygen metabolism during neural stimulation. *J. Cereb. Blood Flow Metab.* 17, 64-72.
- Byatt, G. and Rhodes, G. (1998). Recognition of own-race and other-race caricatures: implications for models of face recognition. *Vision Research* 38, 1455-1468.
- Cabeza, R., Burton, A.M., Kelly, S.W., and Akamatsu, S. (1997). Investigating the relation between imagery and perception: evidence from face priming. *Q. J. Exp. Psychol. A* 50, 274-289.

- Caharel, S., Poiroux, S., Bernard, C., Thibaut, F., Lalonde, R., and Rebai, M. (2003). ERPs associated with familiarity and degree of familiarity during face recognition. *Int J Neurosci* 112, 1499-1512.
- Calder, A.J., Keane, J., Manes, F., Antoun, N., and Young, A.W. (2000). Impaired recognition and experience of disgust following brain injury. *Nature Neuroscience* 3, 1077-1078.
- Calder, A.J., Keane, J., Lawrence, A.D., and Manes, F. (2004). Impaired recognition of anger following damage to the ventral striatum. *Brain* 127, 1958-1969.
- Campanella, S., Hanoteau, C., Depy, D., Rossion, B., Bruyer, R., Crommelinck, M., and Gueri, J.M. (2000). Right N170 modulation in a face discrimination task: an account for categorical perception of familiar faces. *Psychophysiology* 37, 796-806.
- Campanella, S., Quinet, P., Bruyer, R., Cromme, inck, M., and Gueri, J.M. (2002). Categorical perception of happiness and fear facial expression: An ERP study. *Journal of Cognitive Neuroscience* 14, 210-227.
- Campbell, F.W. and Green, D.G. Optical and retinal factors affecting visual resolution. *J Physiol* 181, 576-593. 1965.  
Ref Type: Journal (Full)
- Campbell, R., Elgar, K., Kuntsi, J., Akers, R., Terstegge, J., Coleman, M., and Skuse, D. (2002). The classification of 'fear' from faces is associated with face recognition skill in women. *Neuropsychologia* 40, 575-584.
- Carey, S. and Diamond, R. (1977). From piecemeal to configurational representation of faces. *Science* 195, 312-314.
- Carey, S. (1992). Becoming a face expert. *Philos.Trans.R.Soc.Lond B Biol.Sci.* 335, 95-102.
- Carlesimo, G.A. and Caltagirone, C. (1995). Components in the visual processing of known and unknown faces. *J.Clin.Exp.Neuropsychol.* 17, 691-705.
- Carmel, D. and Bentin, S. (2002). Domain specificity versus expertise: factors influencing distinct processing of faces. *Cognition* 83, 1-29.
- Carton, B. (1875). The electric currents of the brain. *Br.Med.J.* 2, 278.
- Caton, B. (1875). The electric currents of the brain. *Br.Med.J.* 2, 278.
- Christen, L., Landis, T., and Regard, M. (1985). Left hemispheric functional compensation in prosopagnosia? A tachistoscopic study with unilaterally lesioned patients. *Hum.Neurobiol.* 4, 9-14.
- Christie, F. and Bruce, V. (1998). The role of dynamic information in the recognition of unfamiliar faces. *Mem.Cognit.* 26, 780-790.
- Clark, V.P., Keil, K., Maisog, J.M., Courtney, S., Ungerleider, L.G., and Haxby, J.V. (1996). Functional magnetic resonance imaging of human visual cortex during face matching: a comparison with positron emission tomography. *Neuroimage* 4, 1-15.
- Clark, V.P., Maisog, J.M., and Haxby, J.V. (1998). fMRI study of face perception and memory using random stimulus sequences. *J.Neurophysiol.* 79, 3257-3265.
- Clarke, S., Lindemann, A., Maeder, P., Borruat, F.X., and Assal, G. (1997). Face recognition and postero-inferior hemispheric lesions. *Neuropsychologia* 35, 1555-1563.

- Cohn,R., Neumann,M.A., and Wood,D.H. (1974). Prosopagnosia: a clinicopathologic study. *Trans.Am.Neurol.Assoc.* 99, 201-203.
- Cohn,R., Neumann,M.A., and Wood,D.H. (1977). Prosopagnosia: a clinicopathological study. *Ann.Neurol.* 1, 177-182.
- Collishaw,S. and Hole,G.J. (2000). Featural and configurational processes in the recognition of faces of different familiarity. *Perception* 29, 893-909.
- Crane,J. and Milner,B. (2002). Do I know you? Face perception and memory in patients with selective amygdalo-hippocampectomy. *Neuropsychologia* 40, 530-538.
- Critchley,H., Daly,E., Phillips,M., Brammer,M., Bullmore,E., Williams,S., Van Amelsvoort,T., Robertson,D., David,A., and Murphy,D. (2000). Explicit and implicit neural mechanisms for processing of social information from facial expressions: a functional magnetic resonance imaging study. *Human Brain Mapping* 9, 93-105.
- Dailey,M.N. and Cottrell,G.W. (1999). Organization of face and object recognition in modular neural network models. *Neural Netw.* 12, 1053-1074.
- Dailey,M.N. and Cottrell,G.W. (1999). Prosopagnosia in modular neural network models. *Prog.Brain Res.* 121, 165-184.
- Dalgalarondo,P., Fujisawa,G., and Banzato,C.E. (2002). Capgras syndrome and blindness: against the prosopagnosia hypothesis. *Can.J.Psychiatry* 47, 387-388.
- Damasio,A.R., Damasio,H., and Van Hoesen,G.W. (1982). Prosopagnosia: anatomical basis and behavioral mechanisms. *Neurology* 32, 331-341.
- Darwin,C. (1872). *The expression of the emotion in man and animals.* (Oxford: Oxford University Press).
- Das,P., Kemp,A.H., Liddell,B.J., Brown,K.J., Olivieri,G., Peduto,A., Gordon,E., and Williams,L.M. (2005). Pathways for fear perception: modulation of amygdala activity by thalamo-cortical systems. *Neuroimage* 26, 141-148.
- Davidoff,J. and Landis,T. (1990). Recognition of unfamiliar faces in prosopagnosia. *Neuropsychologia* 28, 1143-1161.
- de Gelder,B., Bachoud-Levi,A.C., and Degos,J.D. (1998). Inversion superiority in visual agnosia may be common to a variety of orientation polarised objects besides faces. *Vision Research* 38, 2855-2861.
- de Gelder,B. and Rouw,R. (2000). Configural face processes in acquired and developmental prosopagnosia: evidence for two separate face systems? *Neuroreport* 11, 3145-3150.
- de Gelder,B. and Rouw,R. (2000). Paradoxical configuration effects for faces and objects in prosopagnosia. *Neuropsychologia* 38, 1271-1279.
- de Gelder,B. and Rouw,R. (2000). Structural encoding precludes recognition of face parts in prosopagnosia. *Cognitive Neuropsychology* 17, 89-102.
- de Gelder,B., Pourtois,G., Vroomen,J., and Bachoud-Levi,A.C. (2000). Covert processing of faces in prosopagnosia is restricted to facial expressions: evidence from cross-modal bias. *Brain Cogn* 44, 425-444.

- de Gelder, B. and Rouw, R. (2001). Beyond localization: A dynamical dual route account of face recognition. *Acta Psychologica* 107, 183-207.
- de Gelder, B., Frissen, I., Barton, J.J.S., and Hadjikhani, N. (2003). A modulatory role for facial expressions in prosopagnosia. *Proc. Natl. Acad. Sci. U.S.A* 100, 13105-13110.
- de Haan, E.H., Young, A.W., and Newcombe, F. (1991). Covert and overt recognition in prosopagnosia. *Brain* 114 ( Pt 6), 2575-2591.
- De Renzi, E. (1986). Prosopagnosia in two patients with CT scan evidence of damage confined to the right hemisphere. *Neuropsychologia* 24, 385-389.
- De Renzi, E. (1986). Current issues on prosopagnosia. In *Aspects of Face Processing*, H. D. Ellis, M. A. Jeeves FRSE, F. Newcombe, and A. Young, eds. (Dordrecht / Boston / Lancaster: Martinus Nijhoff Publishers), pp. 243-253.
- De Renzi, E. (1989). [Agnosia]. *Recenti Prog. Med.* 80, 633-637.
- De Renzi, E., Faglioni, P., Grossi, D., and Nichelli, P. (1991). Apperceptive and associative forms of prosopagnosia. *Cortex* 27, 213-221.
- De Renzi, E., Perani, D., Carlesimo, G.A., Silveri, M.C., and Fazio, F. (1994). Prosopagnosia can be associated with damage confined to the right hemisphere--an MRI and PET study and a review of the literature. *Neuropsychologia* 32, 893-902.
- De Renzi, E. and di Pellegrino, G. (1998). Prosopagnosia and alexia without object agnosia. *Cortex* 34, 403-415.
- De Renzi, E. (2000). Disorders of visual recognition. *Semin. Neurol.* 20, 479-485.
- De Valois, R.L. and De Valois, K.K. (1990). *Spatial vision*. (New York: Oxford University press).
- de, G.B. and Stekelenburg, J.J. (2005). Naso-temporal asymmetry of the N170 for processing faces in normal viewers but not in developmental prosopagnosia. *Neurosci. Lett.* 376, 40-45.
- Deichmann, R., Gottfried, J.A., and Turner, R. (2003). Optimized EPI for fMRI studies of the orbitofrontal cortex. *Neuroimage* 19, 430-441.
- Delvenne, J.F., Seron, X., Coyette, F., and Rossion, B. (2004). Evidence for perceptual deficits in associative visual (prosop)agnosia: a single-case study. *Neuropsychologia* 42, 597-612.
- Desimone, R., Albright, T.D., Gross, C.G., and Bruce, C. (1984). Stimulus-selective properties of inferior temporal neurons in the macaque. *J. Neurosci.* 4, 2051-2062.
- Desimone, R. (1991). Face-selective cells in the temporal cortex of monkeys. *Journal of Cognitive Neuroscience* 3, 1-8.
- Di Russo, F., Spinelli, D., and Morrone, M.C. (2001). Automatic gain control contrast mechanisms are modulated by attention in humans: evidence from visual evoked potentials. *Vision Research* 41, 2435-2447.
- Diamond, R. and Carey, S. (1986). Why faces are and are not special: An effect of expertise. *Journal of Experimental Psychology General* 115, 107-117.

- Diamond, B.J., Valentine, T., Mayes, A.R., and Sandel, M.E. (1994). Evidence of covert recognition in a prosopagnosic patient. *Cortex* 30, 377-393.
- Dixon, M.J., Bub, D.N., and Arguin, M. (1998). Semantic and visual determinants of face recognition in a prosopagnosic patient. *Journal of Cognitive Neuroscience* 10, 362-376.
- Dolan, R.J., Fink, G.R., Rolls, E.T., Booth, M., Holmes, A., Frackowiak, R.S.J., and Friston, K.J. (1997). How the brain learns to see objects and faces in an impoverished context. *Nature* 389, 596-569.
- Dolan, R.J. (2002). Emotion, cognition, and behavior. *Science* 298, 1191-1194.
- Dolan, R.J. and Vuilleumier, P. (2003). Amygdala automaticity in emotional processing. *Ann.N.Y.Acad.Sci.* 985, 348-355.
- Duara, R., Phatak, P.G., and Wadia, N.H. (1975). Prosopagnosia and associated disorders. *Neurol.India* 23, 149-155.
- Dubois, S., Rossion, B., Schiltz, C., Bodart, J.M., Michel, C., Bruyer, R., and Crommelinck, M. (1999). Effect of familiarity on the processing of human faces. *Neuroimage* 9, 278-289.
- Duchaine, B.C. (2000). Developmental prosopagnosia with normal configural processing. *Neuroreport* 11, 79-83.
- Duchaine, B.C., Parker, H., and Nakayama, K. (2003). Normal recognition of emotion in a prosopagnosic. *Perception* 32, 827-838.
- Duchaine, B.C. and Weidenfeld, A. (2003). An evaluation of two commonly used tests of unfamiliar face recognition. *Neuropsychologia* 41, 713-720.
- Duchaine, B.C. and Nakayama, K. (2004). Developmental prosopagnosia and Benton recognition test. *Neurology* 62, 1219-1220.
- Duchaine, B.C., Dingle, K., Butterworth, E., and Nakayama, K. (2004). Normal greeble learning in a severe case of developmental prosopagnosia. *Neuron* 43, 469-473.
- Duvernoy, H.M., Delon, S., and Vennson, J.L. (1981). Cortical blood vessels of the human brain. *Brain Res.Bull* 7, 519-579.
- Eger, E., Schyns, P.G., and Kleinschmidt, A. (2004). Scale invariant adaptation in fusiform face-responsive regions. *Neuroimage*. 22, 232-242.
- Eger, E., Henson, R.N., Driver, J., and Dolan, R.J. (2004). BOLD repetition decreases in object-responsive ventral visual areas depend on spatial attention. *J.Neurophysiol.* 92, 1241-1247.
- Eimer, M. (1998). Does the face-specific N170 component reflect the activity of a specialized eye processor? *Neuroreport* 9, 2945-2948.
- Eimer, M. and McCarthy, R.A. (1999). Prosopagnosia and structural encoding of faces: evidence from event-related potentials. *Neuroreport* 10, 255-259.
- Eimer, M. (2000). Event-related brain potentials distinguish processing stages involved in face perception and recognition. *Clinical Neurophysiology* 111, 694-705.
- Eimer, M. (2000). Effects of face inversion on the structural encoding and recognition of faces. Evidence from event-related brain potentials. *Brain Res.Cogn Brain Res.* 10, 145-158.

- Eimer, M. (2000). The face-specific N170 component reflects late stages in the structural encoding of faces. *Neuroreport* 11, 2319-2324.
- Eimer, M. and Holmes, A. (2002). An ERP study on the time course of emotional face processing. *Neuroreport* 13, 427-431.
- Eimer, M., Holmes, A., and McGlone, F.P. (2003). The role of spatial attention in the processing of facial expression: an ERP study of rapid brain responses to six basic emotions. *Cogn Affect.Behav.Neurosci.* 3, 97-110.
- Eimer, M. and Mazza, V. (2005). Electrophysiological correlates of change detection. *Psychophysiology* 42, 328-342.
- Ellis, A.W., Young, A.W., Flude, B.M., and Hay, D.C. (1987). Repetition priming of face recognition. *Q.J.Exp.Psychol.A* 39, 193-210.
- Ellis, A.W., Young, A.W., and Flude, B.M. (1990). Repetition priming and face processing: priming occurs within the system that responds to the identity of a face. *Q.J.Exp.Psychol.A* 42, 495-512.
- Ellis, A.W., Flude, B.M., Young, A., and Burton, A.M. (1996). Two loci of repetition priming in the recognition of familiar faces. *J.Exp.Psychol.Learn.Mem.Cogn* 22, 295-308.
- Ellis, H.D. (1975). Recognizing faces. *Brain Journal of Psychology* 66, 409-426.
- Ellis, H.D. and Young, A.W. (1990). Accounting for delusional misidentifications. *Br.J.Psychiatry* 157, 239-248.
- Ellis, H.D. and Lewis, M.B. (2001). Capgras delusion: a window on face recognition. *TRENDS in Cognitive Science* 5, 149-156.
- Ellison, J.W. and Massaro, D.W. (1997). Featural evaluation, integration, and judgment of facial affect. *Journal of Experimental Psychology: Human Perception & Performance* 23, 213-226.
- Esslen, M., Pascual-Marqui, R.D., Hell, D., Kochi, K., and Lehmann, D. (2004). Brain areas and time course of emotional processing. *Neuroimage* 21, 1189-1203.
- Etcoff, N.L. (1984). Selective attention to facial identity and facial emotion. *Neuropsychologia* 22, 281-295.
- Etcoff, N.L. and Magee, J.J. (1992). Categorical perception of facial expressions. *Cognition* 44, 227-240.
- Ettlin, T.M., Beckson, M., Benson, D.F., Langfitt, J.T., Amos, E.C., and Pineda, G.S. (1992). Prosopagnosia: a bihemispheric disorder. *Cortex* 28, 129-134.
- Evans, J.J., Higgs, A.J., Antoun, N., and Hodges, J.R. (1995). Progressive prosopagnosia associated with selective right temporal lobe atrophy. A new syndrome? *Brain* 118 ( Pt 1), 1-13.
- Farah, M.J., Tanaka, J.W., and Drain, H.M. (1995). What causes the face inversion effect? *J.Exp.Psychol.Hum.Percept.Perform.* 21, 628-634.
- Farah, M.J., Wilson, K.D., Drain, H.M., and Tanaka, J.R. (1995). The inverted face inversion effect in prosopagnosia: evidence for mandatory, face-specific perceptual mechanisms. *Vision Research* 35, 2089-2093.
- Farah, M.J., Levinson, K.L., and Klein, K.L. (1995). Face perception and within-category discrimination in prosopagnosia. *Neuropsychologia* 33, 661-674.

- Farah,M.J., Wilson,K.D., Drain,H.M., and Tanaka,J.N. (1998). What is "special" about face perception? *Psychological Review* 105, 482-498.
- Faulkner,T.F., Rhodes,G., Palermo,R., Pellicano,E., and Ferguson,D. (2002). Recognizing the un-real McCoy: priming and the modularity of face recognition. *Psychonomic Bulletin & Review* 9, 327-334.
- Feinberg,T.E., Rothi,L.J., and Heilman,K.M. (1986). Multimodal agnosia after unilateral left hemisphere lesion. *Neurology* 36, 864-867.
- Fiorentini,A., Maffei,L., and Sandini,G. (1983). The role of high spatial frequencies in face perception. *Perception* 12, 195-201.
- Fried,I., Mateer,C., Ojemann,G., Wohns,R., and Fedio,P. (1982). Organization of visuospatial functions in human cortex. Evidence from electrical stimulation. *Brain* 105, 349-371.
- Fried,I., Cameron,K.A., Yashar,S., Fong,R., and Morrow,J.W. (2002). Inhibitory and excitatory responses of single neurons in the human medial temporal lobe during recognition of faces and objects. *Cerebral Cortex* 12, 575-584.
- Friston,K.J., Williams S.R., Howard,R., Frackowiak,R.S.J., and Turner,R. (1996). Movement-related effects in fMRI time-series. *Magnetic Resonance in Medicine* 35, 346-355.
- Friston,K.J., Fletcher P., Josephs,O., Holmes,A., Rugg,M., and Turner,R. (1998). Event-related fMRI: characterizing differential responses. *Neuroimage* 7, 30-40.
- Friston,K.J., Zarahn,E., Josephs,O., Henson,R.N., and Dale,A.M. (1999). Stochastic designs in event-related fMRI. *Neuroimage*. 10, 607-619.
- Friston,K.J., Zarahn,E., Josephs,O., Henson,R.N., and Dale,A.M. (1999). Stochastic designs in event-related fMRI. *Neuroimage*. 10, 607-619.
- Friston,K.J., Holmes,A., Price,C.J., Buchel,C., and Worsley,K.J. (1999). Multisubject fMRI studies and conjunction analysis. *Neuroimage* 10, 189-210.
- Friston,K.J., Glaser,D.E., Mechelli,A., Turner,R., and Price,C. (2003). Hemodynamic modeling. In *Human Brain Function*, R. S. Frackowiak, K. J. Friston, C. Frith, R. J. Dolan, C. Price, S. Zeki, J. Ashburner, and W. Penny, eds. Academic Press).
- Gainotti,G., Barbier,A., and Marra,C. (2003). Slowly progressive defect in recognition of familiar people in a patient with right anterior temporal atrophy. *Brain* 126, 792-803.
- Ganel,T. and Goshen-Gottstein,Y. (2002). Perceptual integrality of sex and identity of faces: further evidence for the single-route hypothesis. *J.Exp.Psychol.Hum.Percept.Perform.* 28, 854-867.
- Ganel,T. and Goshen-Gottstein,Y. (2004). Effects of familiarity on the perceptual integrality of the identity and expression of faces: the parallel-route hypothesis revisited. *J.Exp.Psychol.Hum.Percept.Perform.* 30, 583-597.
- Gauthier,I., Behrmann,M., and Tarr,M.J. (1999). Can face recognition really be dissociated from object recognition? *Journal of Cognitive Neuroscience* 11, 349-370.
- Gauthier,I., Tarr,M.J., Moylan,J., Skudlaski,P., Gore,J.C., and Anderson,A.W. (2000). The fusiform "face area" is part of a network that processes faces at the individual level. *Journal of Cognitive Neuroscience* 12, 495-504.



- Gauthier, I. and Nelson, C.A. (2001). The development of face expertise. *Current Opinion in Neurobiology* 11, 219-224.
- Gauthier, I. and Palmeri, T.J. (2002). Visual neurons: categorization-based selectivity. *Current Biology* 12, r282-r284.
- Gentileschi, V., Sperber, S., and Spinnler, H. (1999). Progressive defective recognition of familiar people. *Neurocase* 5, 407-424.
- George, N., Dolan, R.J., Fink, G.R., B.G.C., Russel, C., and Driver, J. (1999). Contrast polarity and face recognition in the human fusiform gyrus. *Nature Neuroscience* 2, 574-580.
- George, N., Evans, J., Fiori, N., Davidoff, J., and Renault, B. (1996). Brain events related to normal and moderately scrambled faces. *Brain Res. Cogn Brain Res.* 4, 65-76.
- Gilissen, E. and Zilles, K. (1996). The calcarine sulcus as an estimate of the total volume of human striate cortex: a morphometric study of reliability and intersubject variability. *J.Himforsch.* 37, 57-66.
- Glosser, G., Salvucci, A.E., and Chiaravalloti, N.D. (2003). Naming and recognizing famous faces in temporal lobe epilepsy. *Neurology* 61, 81-86.
- Goffaux, V., Jemel, B., Jacques, C., Rossion, B., and Schyns, P. (2003). ERP evidence for task modulations on face perceptual processing at different spatial scales. *Cognitive Science* 27, 313-325.
- Goffaux, V., Gauthier, I., and Rossion, B. (2003). Spatial scale contribution to early visual differences between face and object processing. *Cognitive Brain Reserach* 16, 416-424.
- Gomez Beldarrain, M.A. (1986). [Prosopagnosia. Bilateral occipital infarct observed in computerized tomography]. *Neurologia* 1, 156-160.
- Gomori, A.J. and Hawryluk, G.A. (1984). Visual agnosia without alexia. *Neurology* 34, 947-950.
- Gorno-Tempini, M.L., Price, C.J., Josephs, O., Vandenberghe, R., Cappa, S.F., Kapur, N., and Frackowiak, R.S.J. (1998). The neural systems sustaining face and proper-name processing. *Brain* 121 (Pt 11), 2103-2118.
- Goshen-Gottstein, Y. and Ganel, T. (2000). Repetition priming for familiar and unfamiliar faces in a sex-judgment task: evidence for a common route for the processing of sex and identity. *J.Exp.Psychol.Learn.Mem.Cogn* 26, 1198-1214.
- Greve, K.W. and Bauer, R.M. (1990). Implicit learning of new faces in prosopagnosia: an application of the mere-exposure paradigm. *Neuropsychologia* 28, 1035-1041.
- Grill-Spector, K., Kushnir, T., Hendler, T., Edelman, S., Itzhak, Y., and Malach, R. (1998). A sequence of object-processing stages revealed by fMRI in the human occipital lobe. *Human Brain Mapping* 6, 316-328.
- Grill-Spector, K., Kushnir, T., Edelman, S., Itzhak, Y., and Malach, R. (1998). Cue-invariant activation in object-related areas of the human occipital lobe. *Neuron* 21, 191-202.
- Grill-Spector, K., Kushnir, T., Edelman, S., Avidan, G., Itzhak, Y., and Malach, R. (1999). Differential processing of objects under various viewing conditions in the human lateral occipital complex. *Neuron* 24, 187-203.

- Grill-Spector,K., Kushnir,T., Hendler,T., and Malach,R. (2000). The dynamics of object-selective activation correlate with recognition performance in humans. *Nature Neuroscience* 3, 837-843.
- Grill-Spector,K. and Malach,R. (2001). fMR-adaptation: a tool for studying the functional properties of human cortical neurons. *Acta Psychol.(Amst)* 107, 293-321.
- Grill-Spector,K., Knouf,N., and Kanwisher,N. (2004). The fusiform face area subserves face perception, not generic within-category identification. *Nat.Neurosci* 7, 555-562.
- Grono-Tempini,M.L. and Price,C. (2001). Identification of famous faces and buildings. *Brain* 124, 2087-2097.
- Gross,C.G. (1992). Representation of visual stimuli in inferior temporal cortex. *Philos.Trans.R.Soc.Lond B Biol.Sci.* 335, 3-10.
- Gross,C.G. and Sergent,J. (1992). Face recognition. *Current Opinion in Neurobiology* 2, 156-161.
- Habib,M. (1986). Visual hypoemotionality and prosopagnosia associated with right temporal lobe isolation. *Neuropsychologia* 24, 577-582.
- Hadjikhani,N. and de Gelder,B. (2002). Neural basis of prosopagnosia: an fMRI study. *Human Brain Mapping* 16, 176-182.
- Haig,N.D. (1984). The effect of feature displacement on face recognition. *Perception* 13, 505-512.
- Haig,N.D. (1986). Exploring recognition with interchanged facial features. *Perception* 15, 235-247.
- Haig,N.D. (1986). High-resolution facial feature saliency mapping. *Perception* 15, 373-386.
- Hamann,S.B., Stefanacci,L., Squire,L.R., Adolphs,R., Tranel,D., Damasio,H., and Damasio,A. (1996). Recognizing facial emotion. *Nature* 379, 497.
- Hamann,S.B. and Adolphs,R. (1999). Normal recognition of emotional similarity between facial expressions following bilateral amygdala damage. *Neuropsychologia* 37, 1135-1141.
- Han,S., Weaver,J.A., Murray,S.O., Kang,X., Yund,W., and Woods,D.L. (2002). Hemispheric asymmetry in global/local processing: effects of stimulus position and spatial frequency. *Neuroimage* 17, 1290-1299.
- Hancock,P.J., Burton,A.M., and Bruce,V. (1996). Face processing: human perception and principal components analysis. *Mem.Cognit.* 24, 21-40.
- Hancock,P.J., Bruce,V., V, and Burton,A.M. (2000). Recognition of unfamiliar faces. *Trends Cogn Sci.* 4, 330-337.
- Harnad,S. (1987). Psychophysical and cognitive aspects of categorical perception: A critical overview. In *Categorical perception: the groundwrok of cognition*, S. Harnad, ed. (New York: Cambridge University Press), pp. 1-25.
- Hashemi,R. and Bradley,G.W. (1997). *MRI the basic*. (Baltimore.
- Hasselmo,M.E., Rolls,E.T., and Baylis,G.C. (1989). The role of expression and identity in the face-selective responses of neurons in the temporal visual cortex of the monkey. *Behav.Brain Res.* 32, 203-218.

- Hasselmo, M.E., Rolls, E.T., Baylis, G.C., and Nalwa, V. (1989). Object-centered encoding by face-selective neurons in the cortex in the superior temporal sulcus of the monkey. *Exp. Brain Res.* 75, 417-429.
- Hasson, U., Hendler, T., Ben Bashat, D., and Malach, R. (2001). Vase or face? A neural correlate of shape-selective grouping processes in the human brain. *J. Cogn. Neurosci.* 13, 744-753.
- Hasson, U., Harel, M., Levy, I., and Malach, R. (2003). Large-scale mirror-symmetry organization of human occipito-temporal areas. *Neuron* 37, 1027-1041.
- Haxby, J.V., Grady, C.L., Horwitz, B., Ungerleider, L.G., Mishkin, M., Carson, R.E., Herscovitch, P., Schapiro, M.B., and Rapoport, S.I. (1991). Dissociation of object and spatial visual processing pathways in human extrastriate cortex. *Proc. Natl. Acad. Sci. U.S.A.* 88, 1621-1625.
- Haxby, J.V., Ungerleider, L.G., Clark, V.P., Schouten, J.L., Hoffman, E.A., and Martin, A. (1999). The effect of face inversion on activity in human neural systems for face and object perception. *Neuron* 22, 189-199.
- Haxby, J.V., Hoffman, E.A., and Gobbini, M.I. (2000). The distributed human neural system for face perception. *TRENDS in Cognitive Science* 4, 223-233.
- Haxby, J.V., Gobbini, M.I., Furey, M.L., Ishai, A., Schouten, J.L., and Pietrini, P. (2001). Distributed and overlapping representations of faces and objects in ventral temporal cortex. *Science* 293, 2425-2430.
- Haxby, J.V., Hoffman, E.A., and Gobbini, M.I. Human neural system for face recognition and social communication. *Biological Psychiatry* 51, 59-67. 2002.  
Ref Type: Journal (Full)
- Hay, D.C. and Young, A. (1982). The human face. In *Normality and pathology in cognitive functions*, A. W. Ellis, ed. (New York: Academic Press).
- Henke, K., Schweinberger, S.R., Grigo, A., Klos, T., and Sommer, W. (1998). Specificity of face recognition: recognition of exemplars of non-face objects in prosopagnosia. *Cortex* 34, 289-296.
- Henson, R.N., Shallice, T., and Dolan, R.J. (2000). Neuroimaging evidence for dissociable forms of repetition priming. *Science* 287, 1269-1272.
- Henson, R.N., Shallice, T., Gorno-Tempini, M.L., and Dolan, R.J. (2002). Face repetition effects in implicit and explicit memory tests as measured by fMRI. *Cerebral Cortex* 12, 178-186.
- Henson, R.N., Goshen-Gottstein, Y., Ganel, T., Otten, L.J., Quayle, A., and Rugg, M.D. (2003). Electrophysiological and haemodynamic correlates of face perception, recognition and priming. *Cerebral Cortex* 13, 793-805.
- Henson, R.N., Cansino, S., Herron, J.E., Robb, W.G., and Rugg, M.D. (2003). A familiarity signal in human anterior medial temporal cortex? *Hippocampus* 13, 301-304.
- Henson, R.N. and Rugg, M.D. (2003). Neural response suppression, haemodynamic repetition effects, and behavioural priming. *Neuropsychologia* 41, 263-270.
- Henson, R.N. (2003). Neuroimaging studies of priming. *Prog. Neurobiol.* 70, 53-81.
- Heywood, C.A. and Cowey, A. (1992). The role of the 'face-cell' area in the discrimination and recognition of faces by monkeys. *Philos. Trans. R. Soc. Lond B Biol. Sci.* 335, 31-37.

- Hibi, Y., Tekeda, Y., and Yagi, A. (2002). Global interference: The effect of Exposure duration that is substituted for spatial frequency. *Perception* 31, 341-348.
- Hietanen, J.K., Perrett, D.I., Oram, M.W., Benson, P.J., and Dittrich, W.H. (1992). The effects of lighting conditions on responses of cells selective for face views in the macaque temporal cortex. *Exp. Brain Res.* 89, 157-171.
- Holmes, A., Vuilleumier, P., and Eimer, M. (2003). The processing of emotional facial expression is gated by spatial attention: evidence from event-related brain potentials. *Brain Res. Cogn Brain Res.* 16, 174-184.
- Horel, J.A. (1993). Retrieval of a face discrimination during suppression of monkey temporal cortex with cold. *Neuropsychologia* 31, 1067-1077.
- Hosie, J.A., Ellis, H.D., and Haig, N.D. (1988). The effect of feature displacement on the perception of well-known faces. *Perception* 17, 461-474.
- Hubel, D.H. and Wiesel, T.N. (1977). Ferrier lecture. Functional architecture of macaque monkey visual cortex. *Proc. R. Soc. Lond B Biol. Sci.* 198, 1-59.
- Hutton, C., Bork, A., Josephs, O., Deichmann, R., Ashburner, J., and Turner, R. (2002). Image distortion correction in fMRI: A quantitative evaluation. *Neuroimage* 16, 217-240.
- Hyder, F., Shulman, R.G., and Rothman, D.L. (1998). A model for the regulation of cerebral oxygen delivery. *J. Appl. Physiol* 85, 554-564.
- Iadecola, C., Yang, G., Ebner, T.J., and Chen, G. (1997). Local and propagated vascular responses evoked by focal synaptic activity in cerebellar cortex. *J. Neurophysiol.* 78, 651-659.
- Iidaka, T., Yamashita, K., Kashikura, K., and Yonekura, Y. (2004). Spatial frequency of visual image modulates neural responses in the temporo-occipital lobe. An investigation with event-related fMRI. *Cognitive Brain Research* 18, 196-204.
- Ishai, A., Haxby, J.V., and Ungerleider, L.G. (2002). Visual imagery of famous faces: Effects of memory and attention revealed by fMRI. *Neuroimage* 17, 1729-1741.
- Itier, R.J. and Taylor, M.J. (2004). N170 or N1? Spatiotemporal Differences between Object and Face Processing Using ERPs. *Cerebral Cortex* 14, 132-142.
- Jasper, H.H. (1958). Appendix to report to committee on clinical examination in EEG: the ten-twenty electrodes system of international federation. *Electroencephalogr. Clin. Neurophysiol.* 10, 371-375.
- Johnson, M.H., Dziurawiec, S., Ellis, H., and Morton, J. (1991). Newborns' preferential tracking of face-like stimuli and its subsequent decline. *Cognition* 40, 1-19.
- Jonsson, J.E. and Hellge, J.B. (1986). Lateralized effects of blurring: a test of the visual spatial frequency model of cerebral hemisphere asymmetry. *Neuropsychologia* 24, 351-362.
- Josephs, O. and Henson, R.N. (1999). Event-related functional magnetic resonance imaging: modelling, inference and optimization. *Philos. Trans. R. Soc. Lond B Biol. Sci.* 354, 1215-1228.
- Josephs, O., Deichmann, R., and Turner, R. (2000). Trajectory measurement and generalised reconstruction in rectilinear EPI. *Neuroimage* 11, S543.

- Joubert,S., Felician,O., Barbeau,E., Sontheimer,A., Barton,J.J.S., Ceccaldi,M., and Poncet,M. (2003). Impaired configurational processing in a case of progressive prosopagnosia associated with predominant right temporal lobe atrophy. *Brain* 126, 2537-2550.
- Kanwisher,N., McDermott,J., and Chun,M.M. (1997). The fusiform face area: A module in human extrastiate cortex specialized for face perception. *The Journal of Neuroscience* 17, 4302-4311.
- Karafin,M.S., Tranel,D., and Adolphs,R. (2004). Dominance attributions following damage to the ventromedial prefrontal cortex. *J.Cogn Neurosci*. 16, 1796-1804.
- Kawahata,N. and Nagata,K. (1989). A case of associative visual agnosia: neuropsychological findings and theoretical considerations. *J.Clin.Exp.Neuropsychol*. 11, 645-664.
- Kawasaki,H., Kaufman,O., Damasio,H., Damasio,A.R., Granner,M., Bakken,H., Hori,T., Howard,M.A., III, and Adolphs,R. (2001). Single-neuron responses to emotional visual stimuli recorded in human ventral prefrontal cortex. *Nat.Neurosci* 4, 15-16.
- Keane,J., Calder,A.J., Hodges,J.R., and Young,A.W. (2002). Face and emotion processing in frontal variant frontotemporal dementia. *Neuropsychologia* 40, 655-665.
- Kendrick,K.M. (1991). How the sheep's brain controls the visual recognition of animals and humans. *J.Anim Sci*. 69, 5008-5016.
- Kiebel,S. and Holmes,A. (2003). The General Linear Model. In *Human Brain Function*, R. S. Frackowiak, K. J. Friston, C. Frith, R. J. Dolan, C. Price, S. Zeki, J. Ashburner, and W. Penny, eds. Academic Press).
- Kiebel,S. and Friston,K.J. (2004). Statistical parametric mapping for event-related potentials II: A hierarchical temporal model. *Neuroimage* 22, 503-520.
- Kiebel,S. and Friston,K.J. (2004). Statistical parametric mapping for event-related potentials I: generic consideration. *Neuroimage* 22, 492-502.
- Kilgour AR, de Gelder,B., and Lessell SJ (2004). Haptic face recognition and prosopagnosia. *Neuropsychologia* 42, 702-712.
- Klopp,J., Halgren,E., Marinkovic,K., and Nenov,V. (1999). Face-selective spectral changes in the human fusiform gyrus. *Clin.Neurophysiol*. 110, 676-682.
- Klopp,J., Marinkovic,K., Chauvel,P., Nenov,V., and Halgren,E. (2000). Early widespread cortical distribution of coherent fusiform face selective activity. *Human Brain Mapping* 11, 286-293.
- Koide,R., Bandoh,M., Isozaki,E., and Hirai,S. (2001). [A case of visual agnosia for picture with right occipital lobe infarction]. *No To Shinkei* 53, 575-579.
- Korner,F., Regli,F., and Haynal,A. (1967). [A form of agnosia characterized by disturbance of color sense, prosopagnosia and orientation disturbance]. *Arch.Psychiatr.Nervenkr*. 209, 1-20.
- Kosslyn,S.M., Hamilton,S.E., and Bernstein,J.H. (1995). The perception of curvature can be selectively disrupted in prosopagnosia. *Brain Cogn* 27, 36-58.
- Kourtzi,Z. and Kanwisher,N. (2000). Representation of perceived object shape by the human lateral occipital complex. *Science* 293, 1506-1509.
- Kreiman,G., Koch,C., and Fried,I. (2000). Category-specific visual responses of single neurons in the human medial temporal lobe. *Nat.Neurosci* 3, 946-953.

- Kreiman, G., Koch, C., and Fried, I. (2000). Imagery neurons in the human brain. *Nature* 408, 357-361.
- Kreiman, G., Fried, I., and Koch, C. (2002). Single-neuron correlates of subjective vision in the human medial temporal lobe. *Proc.Natl.Acad.Sci.U.S.A* 99, 8378-8383.
- Kress, T. and Daum, I. (2003). Event-related potentials reflect impaired face recognition in patients with congenital prosopagnosia. *Neurosci.Lett.* 352, 133-136.
- Krolak-Salmon, P., Henaff, M.A., Vighetto, A., Bertrand, O., and Mauguiere, F. (2004). Early amygdala reaction to fear spreading in occipital, temporal, and frontal cortex: a depth electrode ERP study in human. *Neuron* 42, 665-676.
- Kubo, H., Tsukuda, I., Ando, K., Ishii, H., Miyagi, F., Murata, H., and Yoshida, T. (1978). [A case of cerebral vascular disease associated with prosopagnosia and minor hemisphere syndrome (author's transl)]. *No To Shinkei* 30, 203-209.
- Kucharska-Pietura, K., Phillips, M.L., Gernand, W., and David, A.S. (2003). Perception of emotions from faces and voices following unilateral brain damage. *Neuropsychologia* 41, 1082-1090.
- Kumar, N., Verma, A., Maheshwari, M.C., and Kumar, B.R. (1986). Prosopagnosia (a report of two cases). *J.Assoc.Physicians India* 34, 733-735.
- Kwong, K.K., Belliveau, J.W., Chesler, D.A., Goldberg, D.A., Weiskoff, R.M., Poncelet, B.P., Kennedy, D.N., Hoppel, B.E., Cohen, M.S., Turner, R., Cheng, H.M., Brady, T.J., and Rosen, B.R. (1992). Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation. *Proc.Natl.Acad.Sci.U.S.A* 89, 5675-5679.
- Laeng, B. and Caviness, V.S. (2001). Prosopagnosia as a deficit in encoding curved surface. *Journal of Cognitive Neuroscience* 13, 556-576.
- Lamb, M.R. and Yund, E.W. (1993). The role of spatial frequency in the processing of hierarchically organized stimuli. *Percept.Psychophys.* 54, 773-784.
- Lamb, M.R. and Yund, E.W. (1996). Spatial frequency and attention: effects of level-, target-, and location-repetition on the processing of global and local forms. *Percept.Psychophys.* 58, 363-373.
- Lamb, M.R., Yund, E.W., and Pond, H.M. (1999). Is attentional selection to different levels of hierarchical structure based on spatial frequency? *Journal of Experimental Psychology General* 128, 88-94.
- Lamb, M.R. and Yund, E.W. (2000). The role of spatial frequency in cued shifts of attention between global and local forms. *Percept.Psychophys.* 62, 753-761.
- Lamme, V.A.F. (2001). Blindsight: The role of feedforward and feedback cortical connections. *Acta Psychologica* 107, 209-228.
- Landis, T., Cummings, J.L., Christen, L., Bogen, J.E., and Imhof, H.G. (1986). Are unilateral right posterior cerebral lesions sufficient to cause prosopagnosia? Clinical and radiological findings in six additional patients. *Cortex* 22, 243-252.
- Le Grand, R., Mondloch, C.J., Maurer, D., and Brent, H.P. (2001). Neuropception: Early visual experience and face processing. *Nature* 410, 890.
- Le, S., Raufaste, E., Roussel, S., Puel, M., and Demonet, J.F. (2003). Implicit face perception in a patient with visual agnosia? Evidence from behavioural and eye-tracking analyses. *Neuropsychologia* 41, 702-712.

- Le,S., Raufaste,E., and Demonet,J.F. (2003). Processing of normal, inverted, and scrambled faces in a patient with prosopagnosia: behavioural and eye tracking data. *Brain Res.Cogn Brain Res.* 17, 26-35.
- Leder,H. and Bruce,V. (1998). Local and relational aspects of face distinctiveness. *Q.J.Exp.Psychol.A* 51, 449-473.
- Leder,H. and Bruce,V. (2000). When inverted faces are recognized: the role of configural information in face recognition. *Q.J.Exp.Psychol.A* 53, 513-536.
- Leder,H., Candrian,G., Huber,O., and Bruce,V. (2001). Configural features in the context of upright and inverted faces. *Perception* 30, 73-83.
- Ledes,M., Vortbruggen,J.C., Buhmann,J., Lange,J., von der Malsburg,C., Wurtz,R.P., and Konen,W. (1993). Distortion invariant object recognition in the dynamic link architecture. *IEEE Trans.Computers* 42, 300-311.
- LeDoux,J.E. (1986). Sensory systems and emotion: A model of affective processing. *Integrative Psychiatry* 4, 237-248.
- LeDoux,J.E. (1996). *The emotional brain.* (New york: Simon & Schuster).
- Lee,H.W., Hong,S.B., Seo,D.W., Tae,W.S., and Hong,S.C. (2000). Mapping the functional organization in human visual cortex: Electrical cortical stimulation. *Neurology* 54, 849-859.
- Lee,K., Byatt,G., and Rhodes,G. (2000). Caricature effects, distinctiveness, and identification: testing the face-space framework. *Psychological Science* 11, 379-385.
- Lehky,S.R. (2000). Fine discrimination of faces can be performed rapidly. *Journal of Cognitive Neuroscience* 12, 848-855.
- Leonard,C.M., Rolls,E.T., Wilson,F.A., and Baylis,G.C. (1985). Neurons in the amygdala of the monkey with responses selective for faces. *Behav.Brain Res.* 15, 159-176.
- Leopold,D.A., O'Toole,A.J., Vetter,T., and Blanz,V. (2001). Prototype-referenced shape encoding revealed by high-level aftereffects. *Nature Neuroscience* 4, 89-94.
- Lerner,Y., Hendler,T., Harel,M., and Malach,R. (2001). A hierarchical axis of object processing stages in the human visual cortex. *Cerebral Cortex* 11, 287-297.
- Leveroni,C.L., Seidenberg,M., Mayer,A.R., Mead,L.A., Binder,J.R., and Rao,S.M. (2000). Neural systems underlying the recognition of familiar and newly learned faces. *J.Neurosci.* 20, 878-886.
- Levine,D.N. (1978). Prosopagnosia and visual object agnosia: a behavioral study. *Brain Lang* 5, 341-365.
- Levine,D.N. and Calvanio,R. (1989). Prosopagnosia: a defect in visual configural processing. *Brain Cogn* 10, 149-170.
- Levy,I., Hasson,U., Avidan,G., Hendler,T., and Malach,R. (2001). Center-periphery organization of human object areas. *Nature Neuroscience* 4, 533-539.
- Lhermitte,F., Chain,F., Escourolle,R., Ducarne,B., and Pillon,B. (1972). [Anatomoclinical study of a case of prosopagnosia]. *Rev.Neurol.(Paris)* 126, 329-346.
- Lhermitte,F. and Pillon,B. (1975). [Prosopagnosia. Role of the right hemisphere in visual perception. (Apropos of a case after right occipital lobectomy)]. *Rev.Neurol.(Paris)* 131, 791-812.



- Liddell,B.J., Brown,K.J., Kemp,A.H., Barton,M.J., Das,P., Peduto,A., Gordon,E., and Williams,L.M. (2005). A direct brainstem-amygdala-cortical 'alarm' system for subliminal signals of fear. *Neuroimage* 24, 235-243.
- Lissauer,H. (1890). Ein fall vol seelenblindheit nebst einem beitrage zur theorie derselben [A case of visual agnosia with a contribution of theory]. *Archive fur Psychiatrie* 21, 222-270.
- Liu,J., Harris,A., and Kanwisher,N. (2002). Stages of processing in face perception. *Nature Neuroscience* 5, 910-916.
- Logothetis,N.K., Pauls,J., Augath,M., Trinath,T., and Oeltermann,A. (2001). Neurophysiological investigation of the basis of the fMRI signal. *Nature* 412, 150-157.
- Logothetis,N.K. (2002). The neural basis of the blood-oxygen-level-dependent functional magnetic resonance imaging signal. *Philos.Trans.R.Soc.Lond B Biol.Sci.* 357, 1003-1037.
- Logothetis,N.K. (2003). The underpinnings of the BOLD functional magnetic resonance imaging signal. *J.Neurosci.* 23, 3963-3971.
- Logothetis,N.K. and Wandell,B.A. (2004). Interpreting the BOLD signal. *Annu.Rev.Physiol* 66, 735-769.
- Lopera,F. (2000). [Processing of faces: neurological bases, disorders and evaluation]. *Rev.Neurol.* 30, 486-490.
- Lucas,T.H., Jr., Schoenfield-McNeill,J., Weber,P.B., and Ojemann,G.A. (2003). A direct measure of human lateral temporal lobe neurons responsive to face matching. *Brain Res.Cogn Brain Res.* 18, 15-25.
- Lundqvist,D. and Litton,J.E. The Averaged Karolinska Directed Emotional Faces—AKDEF. 1998.  
Ref Type: Art Work
- Malone,D.R., Morris,H.H., Kay,M.C., and Levin,H.S. (1982). Prosopagnosia: a double dissociation between the recognition of familiar and unfamiliar faces. *Journal of Neurol Neurosurgery Psychiatry* 45, 820-822.
- Mar,D. (1982). *Vision*. (New York: Freeman Publishers).
- Marinkovic,K., Trebon,P., Chauvel,P., and Helgren E (2000). Localized face-processing by the human prefrontal cortex: Face selective intracerebral potentials and post-lesion deficits. *Cognitive Neuropsychology* 17, 187-199.
- Marotta,J.J., Genovese,C.R., and Behrmann,M. (2001). A functional MRI study of face recognition in patients with prosopagnosia. *Neuroreport* 12, 1581-1587.
- Marshall,J.C. and Halligan,P.W. (1988). Blindsight and insight in visuo-spatial neglect. *Nature* 336, 766-767.
- Matsumoto,N., Okada,M., Sugase-Miyamoto,Y., Yamane,S., and Kawano,K. (2004). Population Dynamics of Face-responsive Neurons in the Inferior Temporal Cortex. *Cerebral Cortex*.
- Matsumoto,N., Okada,M., Sugase-Miyamoto,Y., and Yamane,S. (2005). Neuronal mechanisms encoding global-to-fine information in inferior-temporal cortex. *J.Comput.Neurosci.* 18, 85-103.
- Mattout,J., Phillips,C., Penny,W., Rugg,M., and Friston,K.J. (2005). MEG source localization of the M170 using multiple constraints: an extended Bayesian framework. *Neuroimage In Press*.

- Mattson,A.J., Levin,H.S., and Grafman,J. (2000). A case of prosopagnosia following moderate closed head injury with left hemisphere focal lesion. *Cortex* 36, 125-137.
- Maurer,D., Le Grand,R., and Mondloch,C.J. (2002). The many faces of configural processing. *TRENDS in Cognitive Science* 6, 255-260.
- Mäkelä,P., Näsänen,R., Rovamo,J., and Melmoth,D. (2001). Identification of facial images in peripheral vision. *Vision Research* 41, 599-610.
- McCarthy,G., Puce,A., Belger,A., and Allison,T. (1999). Electrophysiological studies of human face preception. II: Response properties of face-specific potentials generated in occipitotemporal cortex. *Cerebral Cortex* 9, 431-444.
- McNeil,J.E. and Warrington,E.K. (1991). Prosopagnosia: a reclassification. *Q.J.Exp.Psychol.A* 43, 267-287.
- McNeil,J.E. and Warrington,E.K. (1993). Prosopagnosia: a face-specific disorder. *Q.J.Exp.Psychol.A* 46, 1-10.
- McNeill,A. and Burton,A.M. (2002). The locus of semantic priming effects in person recognition. *Q.J.Exp.Psychol.A* 55, 1141-1156.
- Meadows,J.C. (1974). The anatomical basis of prosopagnosia. *Journal of Neurol Neurosurgery Psychiatry* 37, 489-501.
- Meeren,H.K., van Heijnsbergen,C.C., and de Gelder,B. (2005). Rapid perceptual integration of facial expression and emotional body language. *Proc.Natl.Acad.Sci.U.S.A* 102, 16518-16523.
- Meletti,S., Benuzzi,F., Rubboli,G., Cantalupo,G., Stanzani,M.M., Nichelli,P., and Tassinari,C.A. (2003). Impaired facial emotion recognition in early-onset right mesial temporal lobe epilepsy. *Neurology* 60, 426-431.
- Mendez,M.F. and Ghajarnia,M. (2001). Agnosia for familiar faces and odors in a patient with right temporal lobe dysfunction. *Neurology* 57, 519-521.
- Mendola,J.D. and Corkin,S. (1999). Visual discrimination and attention after bilateral temporal-lobe lesions: a case study. *Neuropsychologia* 37, 91-102.
- Mendola,J.D., Rizzo,J.F., III, Cosgrove,G.R., Cole,A.J., Black,P., and Corkin,S. (1999). Visual discrimination after anterior temporal lobectomy in humans. *Neurology* 52, 1028-1037.
- Menon,R.S., Ogawa,S., Kim,S.G., Ellermann,J.M., Merkle,H., Tank,D.W., and Ugurbil,K. (1992). Functional brain mapping using MRI: Signal changes accompanying visual stimulation. *Invest.Radiol* 27, S47-S53.
- Mesad,S., Laff,R., and Devinsky,O. (2003). Transient postoperative prosopagnosia. *Epilepsy Behav.* 4, 567-570.
- Michel,F., Perenin,M.T., and Sieroff,E. (1986). [Prosopagnosia without hemianopsia after unilateral right occipitotemporal lesion]. *Rev.Neurol.(Paris)* 142, 545-549.
- Michel,F., Poncet,M., and Signoret,J.L. (1989). [Are the lesions responsible for prosopagnosia always bilateral?]. *Rev.Neurol.(Paris)* 145, 764-770.

- Michelon,P. and Biederman,I. (2003). Less impairment in face imagery than face perception in early prosopagnosia. *Neuropsychologia* 41, 421-441.
- Milders,M.V. and Perrett,D.I. (1993). Recent developments in the neuropsychology and physiology of face processing. *Baillieres Clin.Neurol.* 2, 361-388.
- Morris,J.S., Frith,C.D., Perrett,D.I., Rowland,D., Young,A.W., Calder,A.J., and Dolan,R.J. (1996). A differential neural response in the human amygdala to fearful and happy facial expressions. *Nature* 383, 812-815.
- Morris,J.S., Friston,K.J., Buchel,C., Frith,C.D., Young,A.W., Calder,A.J., and Dolan,R.J. (1998). A neuromodulatory role for the human amygdala in processing emotional facial expressions. *Brain* 121 ( Pt 1), 47-57.
- Morris,J.S., Ohman,A., and Dolan,R.J. (1999). A subcortical pathway to the right amygdala mediating "unseen" fear. *Proc.Natl.Acad.Sci.U.S.A* 96, 1680-1685.
- Morris,J.S., DeGelder,B., Weiskrantz,L., and Dolan,R.J. (2001). Differential extrageniculostriate and amygdala responses to presentation of emotional faces in a cortically blind field. *Brain* 124, 1241-1252.
- Morris,J.S., deBonis,M., and Dolan,R.J. (2002). Human amygdala responses to fearful eyes. *Neuroimage* 17, 214-222.
- Morrison,D.J. and Schyns,P. Less that meets the eye: Interaction between face processing, selective attention and scale perception. submitted.  
Ref Type: Generic
- Morrison,D.J. and Schyns,P. (2001). Usage of spatial scales for the categorization of faces, objects and scenes. *Psychonomic Bulletin & Review* 8, 454-469.
- Morton,J. and Johnson,M.H. (1991). CONSPEC and CONLERN: a two-process theory of infant face recognition. *Psychological Review* 98, 164-181.
- Moscovitch,M., Winocur,G., and Behrmann,M. (1997). What is special about face recognition? Nineteen experiments on a person with visual object agnosia and dyslexia but normal face recognition. *Journal of Cognitive Neuroscience* 9, 555-604.
- Moscovitch,M. and Moscovitch,D.A. (2000). Super face-inversion effects for isolated internal or external features, and fractured faces. *Cognitive Neuropsychology* 17, 201-219.
- Mundel,T., Milton,J.G., Dimitrov,A., Wilson,H.W., Pelizzari,C., Uftiring,S., Torres,I., Erickson,R.K., Spire,J.P., and Towle,V.L. (2003). Transient inability to distinguish between faces: electrophysiologic studies. *J.Clin.Neurophysiol.* 20, 102-110.
- Nardelli,E., Buonanno,F., Coccia,G., Fiaschi,A., Terzian,H., and Rizzuto,N. (1982). Prosopagnosia. Report of four cases. *Eur.Neurol.* 21, 289-297.
- Näsänen,R. (1999). Spatial frequency bandwidth used in the recognition of facial images. *Vision Research* 39, 3824-3833.
- Newcombe,F., Young,A.W., and de Haan,E.H. (1989). Prosopagnosia and object agnosia without covert recognition. *Neuropsychologia* 27, 179-191.
- Newell,F.N., Chiroro,P., and Valentine,T. (1999). Recognizing unfamiliar faces: the effects of distinctiveness and view. *Quarterly Journal of Experimental Psychology - Section A* 52, 509-534.

- NIELSEN, J.M. (1957). Prosopagnosia. *Bull. Los. Angel. Neuro. Soc.* 22, 140-144.
- Nosofsky, R.M. (1986). Attention, similarity, and the identification-categorization relationship. *Journal of Experimental Psychology General* 115, 39-61.
- Nowak, L.G. and Bullier, J. (1997). The timing of information transfer in the visual system. In *Cerebral cortex: Vol. 12. Extrastriate cortex*, J. H. Kaas, K. Rockland, and A. Peters, eds. (New York: Plenum Press), pp. 205-241.
- O'Craven, K.M. and Kanwisher, N. (2000). Mental imagery of faces and places activates corresponding stimulus-specific brain regions. *J. Cogn. Neurosci.* 12, 1013-1023.
- O'Scalaidhe, S.P., Wilson, F.A., and Goldman-Rakic, P.S. (1997). Areal segregation of face-processing neurons in prefrontal cortex. *Science* 278, 1135-1138.
- O'Scalaidhe, S.P., Wilson, F.A., and Goldman-Rakic, P.S. (1999). Face-selective neurons during passive viewing and working memory performance of rhesus monkeys: evidence for intrinsic specialization of neuronal coding. *Cerebral Cortex* 9, 459-475.
- Ogden, J.A. (1993). Visual object agnosia, prosopagnosia, achromatopsia, loss of visual imagery, and autobiographical amnesia following recovery from cortical blindness: case M.H. *Neuropsychologia* 31, 571-589.
- Ojanpää, H. and Näsänen, R. (2003). Utilisation of spatial frequency information in face search. *Vision Research* 43, 2505-2515.
- Ojemann, J.G., Ojemann, G.A., and Lettich, E. (1992). Neuronal activity related to faces and matching in human right nondominant temporal cortex. *Brain* 115 Pt 1, 1-13.
- Olivares, E.I., Iglesias, J., and Antonieta, B.M. (1999). Searching for face-specific long latency ERPs: a topographic study of effects associated with mismatching features. *Brain Res. Cogn. Brain Res.* 7, 343-356.
- Palermo, R. and Rhodes, G. (2002). The influence of divided attention on holistic face perception. *Cognition* 82, 225-257.
- Papagno, C. and Muggia, S. (1999). Naming people ignoring semantics in a patient with left frontal damage. *Cortex* 35, 537-548.
- Parker, D.M., Lishman, J.R., and Hughes, J. Temporal integration of spatially filtered visual images. *Perception* 21, 147-160. 1992.  
Ref Type: Generic
- Parker, D.M., Lishman, J.R., and Hughes, J. (1996). Role of coarse and fine spatial information in face and object processing. *Journal of Experimental Psychology: Human Perception & Performance* 22, 1448-1466.
- Parker, D.M. and Costen, N.P. (1999). One extreme or the other or perhaps the golden mean? Issues of spatial resolution in face processing. *Current Psychology* 18, 118-127.
- Parraga, C.A., Troscianko, T., and Tolhurst, D.J. (2000). The human visual system is optimised for processing the spatial information in natural visual images. *Current Biology* 10, 35-38.
- Pegna, A.J., Khateb, A., Lazeyras, F., and Seghier, M.L. (2005). Discriminating emotional faces without primary visual cortices involves the right amygdala. *Nat. Neurosci* 8, 24-25.

- Penny, W. and Friston, K.J. (2003). Hierarchical models. In *Human Brain Function II*, R. S. J. Frackowiak, K. J. Friston, R. J. Dolan, and J. Ashburner, eds. (London: Elsevier Academic Press), pp. 851-863.
- Peper, M. and Irl, E. (1997). The decoding of emotional concepts in patients with focal cerebral lesions. *Brain Cogn* 34, 360-387.
- Perrett, D., Mistlin, A.J., Chitty, A.J., Harries, M.H., Newcombe, F., and de Haan, E.H. (1988). Neuroanatomical mechanisms of face perception and their pathology. In *Physiological aspects of clinical neuro-ophthamology*, C. Kennard and F. C. Rose, eds. (London: Chapman & Hall), pp. 137-154.
- Perrett, D.I., Rolls, E.T., and Caan, W. (1982). Visual neurones responsive to faces in the monkey temporal cortex. *Exp. Brain Res.* 47, 329-342.
- Perrett, D.I., Smith, P.A., Potter, D.D., Mistlin, A.J., Head, A.S., Milner, A.D., and Jeeves, M.A. (1984). Neurones responsive to faces in the temporal cortex: studies of functional organization, sensitivity to identity and relation to perception. *Hum. Neurobiol.* 3, 197-208.
- Perrett, D.I., Smith, P.A., Potter, D.D., Mistlin, A.J., Head, A.S., Milner, A.D., and Jeeves, M.A. (1985). Visual cells in the temporal cortex sensitive to face view and gaze direction. *Proc. R. Soc. Lond B Biol. Sci.* 223, 293-317.
- Perrett, D.I., Oram, M.W., Harries, M.H., Bevan, R., Hietanen, J.K., Benson, P.J., and Thomas, S. (1991). Viewer-centred and object-centred coding of heads in the macaque temporal cortex. *Exp. Brain Res.* 86, 159-173.
- Perrett, D.I., Hietanen, J.K., Oram, M.W., and Benson, P.J. (1992). Organization and functions of cells responsive to faces in the temporal cortex. *Philos. Trans. R. Soc. Lond B Biol. Sci.* 335, 23-30.
- Pessa, E., Bandinelli, P.L., and Penna, M.P. (1999). Simulating prosopagnosia through a lesion of lateral connections in a feed-forward neural network. *Ital. J. Neurol. Sci.* 20, 29-36.
- Pessoa, L. (2005). To what extent are emotional visual stimuli processed without attention and awareness? *Current Opinion in Neurobiology* 15, 188-196.
- Phillips, M.L., Young, A.W., Senior, C., Brammer, M., Andrew, C., Calder, A.J., Bullmore, E.T., Perrett, D.I., Rowland, D., Williams, S.C., Gray, J.A., and David, A.S. (1997). A specific neural substrate for perceiving facial expressions of disgust. *Nature* 389, 495-498.
- Phillips, M.L., Bullmore, E.T., Howard, R., Woodruff, P.W., Wright, I.C., Williams, S.C., Simmons, A., Andrew, C., Brammer, M., and David, A.S. (1998). Investigation of facial recognition memory and happy and sad facial expression perception: an fMRI study. *Psychiatry Res.* 83, 127-138.
- Phillips, M.L., Young, A.W., Scott, S.K., Calder, A.J., Andrew, C., Giampietro, V., Williams, S.C., Bullmore, E.T., Brammer, M., and Gray, J.A. (1998). Neural responses to facial and vocal expressions of fear and disgust. *Proc. Biol. Sci.* 265, 1809-1817.
- Phillips, M.L., Medford, N., Young, A.W., Williams, L., Williams, S.C., Bullmore, E.T., Gray, J.A., and Brammer, M.J. (2001). Time courses of left and right amygdalar responses to fearful facial expressions. *Human Brain Mapping* 12, 193-202.
- Phillips, M.L., Williams, L.M., Heining, M., Herba, C.M., Russell, T., Andrew, C., Bullmore, E.T., Brammer, M.J., Williams, S.C., Morgan, M., Young, A.W., and Gray, J.A. (2004). Differential neural responses to overt and covert presentations of facial expressions of fear and disgust. *Neuroimage* 21, 1484-1496.

- Pigarev, I.N., Rizzolatti, G., and Scandolara, C. (1979). Neurons responding to visual stimuli in the frontal lobe of macaque monkeys. *Neurosci.Lett.* 12, 207-212.
- Poline, J.B., Kherif, F., and Penny, W. (2003). Contrast and classical inference. In *Human Brain Function*, R. S. Frackowiak, K. J. Friston, C. Frith, R. J. Dolan, C. Price, S. Zeki, J. Ashburner, and W. Penny, eds.
- Polster, M.R. and Rapcsak, S.Z. (1996). Representations in learning new faces: evidence from prosopagnosia. *J.Int.Neuropsychol.Soc.* 2, 240-248.
- Posamentier, M.T. and Abdi, H. (2003). Processing faces and facial expressions. *Neuropsychol.Rev.* 13, 113-143.
- Pourtois, G., Grandjean, D., Sander, D., and Vuilleumier, P. (2004). Electrophysiological correlates of rapid spatial orienting towards fearful faces. *Cerebral Cortex* 14, 619-633.
- Pradat-Diehl, P., Chevignard, M., and Peskine, A. (2003). [Semiology of sensorial integration: visual disorders of cerebral origin]. *Rev.Prat.* 53, 371-376.
- Pratesi, M., Santini, S., Lombardo, G., Corsi, P., Salvadori, G., and Cocco, F. (1992). [Prosopagnosia. Description and discussion of a clinical case]. *Recenti Prog.Med.* 83, 282-285.
- Price, C.J., Velzman, D.J., Ashburner, J., Josephs, O., and Friston, K.J. (1999). The critical relationship between the timing of stimulus presentation and data acquisition in blocked designs with fMRI. *Neuroimage* 10, 36-44.
- Puce, A., Allison, T., and McCarthy, G. (1995). Face-sensitive regions in human extrastriate cortex by functional MRI. *Journal of Neurophysiology* 74, 1192-1199.
- Puce, A., Allison, T., and McCarthy, G. (1999). Electrophysiological studies of human face perception. III: Effects of top-down processing on face-specific potentials. *Cerebral Cortex* 9, 445-458.
- Quaglino, A., Borelli, G.B., Della, S.S., and Young, A.W. (2003). Quaglino's 1867 case of prosopagnosia. *Cortex* 39, 533-540.
- Quiroga, R.Q., Reddy, L., Kreiman, G., Koch, C., and Fried, I. (2005). Invariant visual representation by single neurons in the human brain. *Nature* 435, 1102-1107.
- Ranganath, C. and D'Esposito, M. (2001). Medial temporal lobe activity associated with active maintenance of novel information. *Neuron* 31, 865-873.
- Rapcsak, S.Z., Polster, M.R., Glisky, M.L., and Comer, J.F. (1996). False recognition of unfamiliar faces following right hemisphere damage: neuropsychological and anatomical observations. *Cortex* 32, 593-611.
- Rapcsak, S.Z., Galper, S.R., Comer, J.F., Reminger, S.L., Nielsen, L., Kaszniak, A.W., Verfaellie, M., Laguna, J.F., Labiner, D.M., and Cohen, R.A. (2000). Fear recognition deficits after focal brain damage: a cautionary note. *Neurology* 54, 575-581.
- Rapcsak, S.Z., Nielsen, L., Littrell, L.D., Glisky, E.L., Kaszniak, A.W., and Laguna, J.F. (2001). Face memory impairments in patients with frontal lobe damage. *Neurology* 57, 1168-1175.
- Rees, G., Howseman, A., Josephs, O., Frith, C.D., Friston, K.J., Frackowiak, R.S., and Turner, R. (1997). Characterizing the relationship between BOLD contrast and regional cerebral blood flow measurements by varying the stimulus presentation rate. *Neuroimage* 6, 270-278.

- Reinvang,I., Magnussen,S., and Greenlee,M.W. (2002). Hemispheric asymmetry in visual discrimination and memory: ERP evidence for the spatila frequency hypothesis. *Experimental Brain Research* 144, 483-495.
- Renault,B., Signoret,J.L., Debruille,B., Breton,F., and Bolgert,F. (1989). Brain potentials reveal covert facial recognition in prosopagnosia. *Neuropsychologia* 27, 905-912.
- Rentschler,I., Treutwein,B., and Landis,T. (1994). Dissociation of local and global processing in visual agnosia. *Vision Research* 34, 963-971.
- Rhodes,G. (1988). Looking at faces: First-order and second-order features as determinates of facial appearance. *Perception* 17, 43-63.
- Rhodes,G., Brake,S., and Atkinson,A.P. (1993). What's lost in inverted faces? *Cognition* 47, 25-47.
- Rhodes,G., Byatt,G., Tremewan,T., and Kennedy,A. (1997). Facial distinctiveness and the power of caricatures. *Perception* 26, 207-223.
- Rhodes,G., Byatt,G., Michie,P.T., and Puce,A. (2004). Is the fusiform face area specialized for faces, individuation, or expert individuation? *J.Cogn Neurosci.* 16, 189-203.
- Rizzo,M., Corbett,J.J., Thompson,H.S., and Damasio,A.R. (1986). Spatial contrast sensitivity in facial recognition. *Neurology* 36, 1254-1256.
- Robson,M.D., Doroz,J.L., and Gore,J.C. (1998). Measurements of the temporal fMRI response of the human auditory cortex to trains of tones. *Neuroimage* 7, 185-189.
- Rolls,E.T. (1984). Neurons in the cortex of the temporal lobe and in the amygdala of the monkey with responses selective for faces. *Hum.Neurobiol.* 3, 209-222.
- Rolls,E.T., Baylis,G.C., and Leonard,C.M. (1985). Role of low and high spatial frequencies in the face-selective responses of neurons in the cortex in the superior temporal sulcus in the monkey. *Vision Research* 25, 1021-1035.
- Rolls,E.T. and Baylis,G.C. (1986). Size and contrast have only small effects on the responses to faces of neurons in the cortex of the superior temporal sulcus of the monkey. *Exp.Brain Res.* 65, 38-48.
- Rolls,E.T., Baylis,G.C., and Hasselmo,M.E. (1987). The responses of neurons in the cortex in the superior temporal sulcus of the monkey to band-pass spatial frequency filtered faces. *Vision Research* 27, 311-326.
- Rolls,E.T. and Williams,G.V. (1987). Sensory and movement-related neuronal activity in different regions of the primate striatum. In *Basal Ganglia and Behavior: Sensory Aspects and Motor Functioning*, J. S. Schneider and T. I. Lidsky, eds. (Berlin: Hans Huber), pp. 37-59.
- Rolls,E.T., Baylis,G.C., Hasselmo,M.E., and Nalwa,V. (1989). The effect of learning on the face selective responses of neurons in the cortex in the superior temporal sulcus of the monkey. *Exp.Brain Res.* 76, 153-164.
- Rolls,E.T. (1992). Neurophysiological mechanisms underlying face processing within and beyond the temporal cortical visual areas. *Philos.Trans.R.Soc.Lond B Biol.Sci.* 335, 11-20.
- Rolls,E.T., Tovee,M.J., Purcell,D.G., Stewart,A.L., and Azzopardi,P. (1994). The responses of neurons in the temporal cortex of primates, and face identification and detection. *Exp.Brain Res.* 101, 473-484.



- Rolls, E.T., Treves, A., and Tovee, M.J. (1997). The representational capacity of the distributed encoding of information provided by populations of neurons in primate temporal visual cortex. *Exp. Brain Res.* 114, 149-162.
- Rolls, E.T. (1999). *The brain and emotion*. (Oxford: Oxford University Press).
- Rosler, A., Lanquillon, S., Dippel, O., and Braune, H.J. (1997). Impairment of facial recognition in patients with right cerebral infarcts quantified by computer aided "morphing". *Journal of Neurol Neurosurgery Psychiatry* 62, 261-264.
- Rossion, B., Delvenne, J.F., Debatisse, D., Goffaux, V., Bruyer, R., Crommelinck, M., and Guerit, J.M. (1999). Spatio-temporal localization of the face inversion effect: an event-related potentials study. *Biol. Psychol.* 50, 173-189.
- Rossion, B., Campanella, S., Gomez, C.M., Delinte, A., Debatisse, D., Liard, L., Dubois, S., Bruyer, R., Crommelinck, M., and Guerit, J.M. (1999). Task modulation of brain activity related to familiar and unfamiliar face processing: an ERP study. *Clinical Neurophysiology* 110, 449-462.
- Rossion, B., Dricot, L., Devolder, A., Bodart, J.M., Crommelinck, M., de Gelder, B., and Zoontjes, R. (2000). Hemispheric asymmetries for whole-based and part-based face processing in the human fusiform gyrus. *Journal of Cognitive Neuroscience* 12, 793-802.
- Rossion, B., Schiltz, C., Robaye, L., Pirenne, D., and Crommelinck, M. (2001). How does the brain discriminate familiar and unfamiliar faces?: a PET study of face categorical perception. *Journal of Cognitive Neuroscience* 13, 1019-1034.
- Rossion, B., Caldara, R., Seghier, M., Schuller, A., Lazeyras, F., and Mayer, E. (2003). A network of occipito-temporal face sensitive areas beside the right middle fusiform gyrus is necessary for normal face processing. *Brain* 126, 1-15.
- Rossion, B., Schiltz, C., and Crommelinck, M. (2003). The functionally defined right occipital and fusiform "face areas" discriminate novel from visually familiar faces. *Neuroimage* 19, 877-883.
- Rotshtein, P., Malach, R., Hadar, U., Graif, M., and Hendler, T. (2001). Feeling or features: different sensitivity to emotion in high-order visual cortex and amygdala. *Neuron* 32, 747-757.
- Rotshtein, P., Henson, R.N., Treves, A., Driver, J., and Dolan, R.J. (2005). Morphing Marilyn into Maggie dissociates physical and identity face representations in the brain. *Nat. Neurosci* 8, 107-113.
- Rotshtein, P., Henson, R.N., Treves, A., Driver, J., and Dolan, R.J. (2005). Morphing Marilyn into Maggie dissociates physical and identity face-representations in the brain. *Nature Neuroscience* *In press*.
- Sagiv, N. and Bentin, S. (2001). Structural encoding of human and schematic faces: Holistic and part based processes. *Journal of Cognitive Neuroscience* 13, 937-951.
- Sakai, K. and Passingham, R.E. (2003). Prefrontal interactions reflect future task operations. *Nature Neuroscience* 6, 75-81.
- Sala, S. and Young, A.W. (2003). Quaglino's 1867 case of prosopagnosia. *Cortex* 39, 533-40.
- Sato, W., Kochiyama, T., Yoshikawa, S., and Matsumura, M. (2001). Emotional expression boosts early visual processing of the face: ERP recording and its decomposition by independent component analysis. *Neuroreport* 12, 709-714.

- Saumier,D., Arguin,M., and Lassonde,M. (2001). Prosopagnosia: a case study involving problems in processing configural information. *Brain Cogn* 46, 255-259.
- Schuz,A. and Palm,G. (1989). Density of neurons and synapses in the cerebral cortex of the mouse. *J.Comp.Neurol.* 286, 442-445.
- Schwartz,C.E., Wright,C.I., Shin,L.M., Kagan,J., Whalen,P.J., McMullin,K.G., and Rauch,S.L. (2003). Differential amygdalar response to novel versus newly familiar neutral faces: a functional MRI probe developed for studying inhibited temperament. *Biological Psychiatry* 53, 854-862.
- Schweinberger,S.R., Klos,T., and Sommer,W. (1995). Covert face recognition in prosopagnosia: a dissociable function? *Cortex* 31, 517-529.
- Schweinberger,S.R., Burton,A.M., and Kelly,S.W. (1999). Asymmetric dependencies in perceiving identity and emotion: experiments with morphed faces. *Percept.Psychophys.* 61, 1102-1115.
- Schweinberger,S.R., Pickering,E.C., Burton,A.M., and Kaufmann,J.M. (2002). Human brain potential correlates of repetition priming in face and name recognition. *Neuropsychologia* 40, 2057-2073.
- Schweinberger,S.R., Pickering,E.C., Jentsch,I., Burton,A.M., and Kaufmann,J.M. (2002). Event-related brain potential evidence for a response of inferior temporal cortex to familiar face repetitions. *Brain Res.Cogn Brain Res.* 14, 398-409.
- Schweinberger,S.R., Huddy,V., and Burton,A.M. (2004). N250r: a face-selective brain response to stimulus repetitions. *Neuroreport* 15, 1501-1505.
- Schyns,P. and Oliva,A. (1999). Dr. angry and Mr. Smile: When categorization flexibly modifies the perception of faces in rapid visual presentations. *Cognition* 69, 243-265.
- Seeck,M. and Grusser,O.J. (1992). Category-related components in visual evoked potentials: photographs of faces, persons, flowers and tools as stimuli. *Exp.Brain Res.* 92, 338-349.
- Seeck,M., Mainwaring,N., Ives,J., Blume,H., Dubuisson,D., Cosgrove,R., Mesulam,M.M., and Schomer,D.L. (1993). Differential neural activity in the human temporal lobe evoked by faces of family members and friends. *Ann.Neurol.* 34, 369-372.
- Seeck,M., Schomer,D., Mainwaring,N., Ives,J., Dubuisson,D., Blume,H., Cosgrove,R., Ransil,B.J., and Mesulam,M.M. (1995). Selectively distributed processing of visual object recognition in the temporal and frontal lobes of the human brain. *Ann.Neurol.* 37, 538-545.
- Seeck,M., Michel,C.M., Mainwaring,N., Cosgrove,R., Blume,H., Ives,J., Landis,T., and Schomer,D.L. (1997). Evidence for rapid face recognition from human scalp and intracranial electrodes. *Neuroreport* 8, 2749-2754.
- Seeck,M., Mainwaring,N., Cosgrove,R., Blume,H., Dubuisson,D., Mesulam,M.M., and Schomer,D.L. (1997). Neurophysiologic correlates of implicit face memory in intracranial visual evoked potentials. *Neurology* 49, 1312-1316.
- Seeck,M., Michel,C.M., Blanke,O., Thut,G., Landis,T., and Schomer,D.L. (2001). Intracranial Neurophysiological Correlates Related to the Processing of Faces. *Epilepsy Behav.* 2, 545-557.
- Seidenberg,M., Griffith,R., Sabsevitz,D., Moran,M., haltiner,A., Bell,B., Swanson,S., Hammeke,T., and Hermann,B. (2002). Recognition and identification of famous faces in patients with unilateral temporal lobe epilepsy. *Neuropsychologia* 40, 446-456.

- Sekuler, A.B., Gaspar, C.M., Gold, J.M., and Bennett, P.J. (2004). Inversion leads to quantitative, not qualitative, changes in face processing. *Curr.Biol.* 14, 391-396.
- Semenza, C., Sartori, G., and D'Andrea, J. (2003). He can tell which master craftsman blew a Venetian vase, but he can not name the Pope: a patient with a selective difficulty in naming faces. *Neurosci.Lett.* 352, 73-75.
- Sergent, J. (1984). An investigation into component and configural processes underlying face perception. *British Journal of Psychology* 75, 221-242.
- Sergent, J. (1984). Configural processing of faces in the left and right cerebral hemispheres. *Journal of Experimental Psychology: Human Perception & Performance* 10, 554-572.
- Sergent, J. and Villemure, J.G. (1989). Prosopagnosia in a right hemispherectomized patient. *Brain* 112 ( Pt 4), 975-995.
- Sergent, J. and Poncet, M. (1990). From covert to overt recognition of faces in a prosopagnosic patient. *Brain* 113 ( Pt 4), 989-1004.
- Sergent, J. and Signoret, J.L. (1992). Varieties of functional deficits in prosopagnosia. *Cerebral Cortex* 2, 375-388.
- Sergent, J. and Signoret, J.L. (1992). Functional and anatomical decomposition of face processing: evidence from prosopagnosia and PET study of normal subjects. *Philos.Trans.R.Soc.Lond B Biol.Sci.* 335, 55-61.
- Sergent, J., Ohta, S., and McDonald, B. (1992). Functional neuroanatomy of face and object processing: a positron emission tomography study. *Brain* 115, 15-36.
- Sergent, J. and Signoret, J.L. (1992). Implicit access to knowledge derived from unrecognized faces in prosopagnosia. *Cerebral Cortex* 2, 389-400.
- Shah, N.J., Marshall, J.C., Zafiris, O., Schwab, A., Markowitsch, H.J., and Fink, G.R. (2001). The neural correlates of person familiarity. A functional magnetic resonance imaging study with clinical implications. *Brain* 124, 804-815.
- Shipp, S. and Zeki, S. (1995). Segregation and convergence of specialised pathways in macaque monkey visual cortex. *J Anat* 187, 547-562.
- Shipp, S. (2001). Corticopulvinar connections of areas V5, V4, and V3 in the macaque monkeys: A dual model of retinal and cortical topographic. *The Journal of Comparative Neurology* 439, 469-490.
- SHOLL, D.A. (1956). The measurable parameters of the cerebral cortex and their significance in its organization. *Prog.Neurobiol.* 324-333.
- Siebert, M., Markowitsch, H.J., and Bartel, P. (2003). Amygdala, affect and cognition: evidence from 10 patients with Urbach-Wiethe disease. *Brain* 126, 2627-2637.
- Sigala, N. and Logothetis, N.K. (2002). Visual categorization shapes feature selectivity in the primate temporal cortex. *Nature* 415, 318-320.
- Singh, K.D., Smith, A.T., and Greenlee, M.W. (2000). Spatiotemporal frequency and direction sensitivities of human visual areas measured using fMRI. *Neuroimage* 12, 550-564.

- Sirovich, L. and Kirby, M. (1987). Low-dimensional procedure for the characterization of human faces. *J. Opt Soc Am* 4, 519-524.
- Skottun, B.C. The magnocellular deficit theory of dyslexia: the evidence from contrast sensitivity. *Vision Research* 40, 111-127. 2000.  
Ref Type: Generic
- Small, M. (1988). Visual evoked potentials in a patient with prosopagnosia. *Electroencephalogr. Clin. Neurophysiol.* 71, 10-16.
- Smith, M.L., Gosselin, F., and Schyns, P.G. (2004). Receptive fields for flexible face categorizations. *Psychological Science* 15, 753-761.
- Snowden, J.S., Thompson, J.C., and Neary, D. (2004). Knowledge of famous faces and names in semantic dementia. *Brain* 127, 860-872.
- Solms, M., Kaplan-Solms, K., and Brown, K.J. (1996). Wilbrand 1892. In *Classical case in neuropsychologia*, A. Code, ed. (Erlbaum: Hove), pp. 89-110.
- Sperber, S. and Spinnler, H. (2003). Covert person recognition: its fadeout in a case of temporal lobe degeneration. *Cortex* 39, 57-67.
- Spillmann, L., Laskowski, W., Lange, K.W., Kasper, E., and Schmidt, D.D. (2000). Stroke-blind for colors, faces and locations: Partial recovery after three years. *Restor. Neurol. Neurosci.* 17, 89-103.
- Stone, A. and Valentine, T. (2003). Perspectives on prosopagnosia and models of face recognition. *Cortex* 39, 31-40.
- Streit, M., Brinkmeyer, J., Wolwer, W., and Gaebel, W. (2003). EEG brain mapping in schizophrenic patients and healthy subjects during facial emotion recognition. *Schizophr. Res.* 61, 121-122.
- Sugase, Y., Yamane, S., Ueno, S., and Kawano, K. (1999). Global and fine information coded by single neurons in the temporal visual cortex. *Nature* 400, 869-873.
- Sugiura, M., Kawashima, R., Nakamura, K., Sato, N., Nakamura, A., Kato, T., Hatano, K., Schormann, T., Zilles, K., Sato, K., Ito, K., and Fukuda, H. (2001). Activation reduction in anterior temporal cortices during repeated recognition of faces of personal acquaintances. *Neuroimage* 13, 877-890.
- Surguladze, S.A., Brammer, M.J., Young, A.W., Andrew, C., Travis, M.J., Williams, S.C., and Phillips, M.L. (2003). A preferential increase in the extrastriate response to signals of danger. *Neuroimage* 19, 1317-1328.
- Tagawa, K., Nagata, K., and Shishido, F. (1990). Occipital lobe infarction and positron emission tomography. *Tohoku J. Exp. Med.* 161 Suppl, 139-153.
- Takahashi, N., Kawamura, M., Hirayama, K., and Tagawa, K. (1989). [Non-verbal facial and topographic visual object agnosia--a problem of familiarity in prosopagnosia and topographic disorientation]. *No To Shinkei* 41, 703-710.
- Takahashi, N., Kawamura, M., Hirayama, K., Shiota, J., and Isono, O. (1995). Prosopagnosia: a clinical and anatomical study of four patients. *Cortex* 31, 317-329.
- Tanaka, J., Giles, M., Kremen, S., and Simon, V. (1998). Mapping attractor fields in face space: the atypicality bias in face recognition. *Cognition* 68, 199-220.

- Tanaka, J.W. and Farah, M.J. (1991). Second-order relational properties and the inversion effect: testing a theory of face perception. *Percept. Psychophys.* 50, 367-372.
- Tanaka, J.W. and Farah, M.J. (1993). Parts and wholes in face recognition. *Q. J. Exp. Psychol. A* 46, 225-245.
- Tanaka, J.W. and Sengco, J.A. (1997). Features and their configuration in face recognition. *Mem. Cognit.* 25, 583-592.
- Tanaka, K., Saito, H., Fukada, Y., and Mori, M. (1991). Coding visual images of objects in the inferotemporal cortex of the macaque monkey. *Journal of Neurophysiology* 66, 170-189.
- Tarr, M.J. and Gauthier, I. (2000). FFA: a flexible fusiform area for subordinate-level visual processing automatized by expertise. *Nature Neuroscience* 3, 746-749.
- Tiippana, K., Rovamo, J., Näsänen, R., Whitaker, A., and Mäkelä, P. (2000). Contrast matching across spatial frequencies for isoluminant chromatic gratings. *Vision Research* 40, 2159-2165.
- Tiippana, K. and Näsänen, R. (2003). Spatial-frequency bandwidth of perceived contrast. *Vision Research* 39, 3399-3403.
- Tohgi, H., Watanabe, K., Takahashi, H., Yonezawa, H., Hatano, K., and Sasaki, T. (1994). Prosopagnosia without topographagnosia and object agnosia associated with a lesion confined to the right occipitotemporal region. *J. Neurol.* 241, 470-474.
- Tovee, M.J., Rolls, E.T., Treves, A., and Bellis, R.P. (1993). Information encoding and the responses of single neurons in the primate temporal visual cortex. *J. Neurophysiol.* 70, 640-654.
- Tovee, M.J., Rolls, E.T., and Azzopardi, P. (1994). Translation invariance in the responses to faces of single neurons in the temporal visual cortical areas of the alert macaque. *J. Neurophysiol.* 72, 1049-1060.
- Tranel, D. and Damasio, A.R. (1985). Knowledge without awareness: an autonomic index of facial recognition by prosopagnosics. *Science* 228, 1453-1454.
- Tranel, D., Damasio, H., and Damasio, A.R. (1997). A neural basis for the retrieval of conceptual knowledge. *Neuropsychologia* 35, 1319-1327.
- Treves, A., Panzeri, S., Rolls, E.T., Booth, M., and Waksman, E.A. (1999). Firing rate distributions and efficiency of information transmission of inferior temporal cortex neurons to natural visual stimuli. *Neural Comput.* 11, 601-632.
- Trobe, J.R. and Bauer, R.M. (1986). Seeing but not recognizing. *Surv. Ophthalmol.* 30, 328-336.
- Tsao, D.Y., Freiwald, W.A., Knutsen, T.A., Mandeville, J.B., and Tootell, R.B. (2003). Faces and objects in macaque cerebral cortex. *Nature Neuroscience* 6, 989-995.
- Uttner, I., Bliem, H., and Danek, A. (2002). Prosopagnosia after unilateral right cerebral infarction. *J. Neurol.* 249, 933-935.
- Valentine, T. and Bruce, V. (1985). What's up? The Margaret Thatcher illusion revisited. *Perception* 14, 515-516.
- Valentine, T. and Bruce, V. (1986). Recognizing familiar faces: the role of distinctiveness and familiarity. *Can. J. Psychol.* 40, 300-305.

- Valentine, T. and Bruce, V. (1986). The effect of race, inversion and encoding activity upon face recognition. *Acta Psychol. (Amst)* 61, 259-273.
- Valentine, T. and Bruce, V. (1986). The effects of distinctiveness in recognising and classifying faces. *Perception* 15, 525-535.
- Valentine, T. and Bruce, V. (1988). Mental rotation of faces. *Mem. Cognit.* 16, 556-566.
- Valentine, T. (1991). A unified account of the effects of distinctiveness, inversion and race in face recognition. *Quarterly Journal of Experimental Psychology - Section A* 43, 161-204.
- Valentine, T. and Endo, M. (1992). Towards an exemplar of face processing: The effects of race and distinctiveness. *Quarterly Journal of Experimental Psychology - Section A* 44, 671-703.
- Verstichel, P. and Chia, L. (1999). [Difficulties in face identification after lesion in the left hemisphere]. *Rev. Neurol. (Paris)* 155, 937-943.
- Verstichel, P. (2001). [Impaired recognition of faces: implicit recognition, feeling of familiarity, role of each hemisphere]. *Bull. Acad. Natl. Med.* 185, 537-549.
- Viggiano, M.P. (1996). Event-related potentials in brain-injured patients with neuropsychological disorders: a review. *J. Clin. Exp. Neuropsychol.* 18, 631-647.
- Vignal, J.P., Chauvel, P., and Helgren E (2000). Localised face processing by the human prefrontal cortex: Stimulation-evoked hallucinations of faces. *Cognitive Neuropsychology* 17, 281-291.
- Vuilleumier, P., Armony, J.L., Driver, J., and Dolan, R.J. (2001). Effects of attention and emotion on face processing in the human brain: an event-related fMRI study. *Neuron* 30, 829-841.
- Vuilleumier, P., Armony, J.L., Clarke, K., Husain, M., Driver, J., and Dolan, R.J. (2002). Neural response to emotional faces with and without awareness: event-related fMRI in a parietal patient with visual extinction and spatial neglect. *Neuropsychologia* 40, 2156-2166.
- Vuilleumier, P., Armony, J.L., Driver, J., and Dolan, R.J. (2003). Distinct spatial frequency sensitivities for processing faces and emotional expressions. *Nature Neuroscience* 6, 624-631.
- Vuilleumier, P., Richardson, M.P., Armony, J.L., Driver, J., and Dolan, R.J. (2004). Distant influences of amygdala lesion on visual cortical activation during emotional face processing. *Nature Neuroscience* 7, 1271-1278.
- Wacholtz, E. (1996). Can we learn from the clinically significant face processing deficits, prosopagnosia and Capgras delusion? *Neuropsychol. Rev.* 6, 203-257.
- Wada, Y. and Yamamoto, T. (2001). Selective impairment of facial recognition due to a haematoma restricted to the right fusiform and lateral occipital region. *Journal of Neurol Neurosurgery Psychiatry* 71, 254-257.
- Ward, J. and Jones, L. (2003). Inappropriate association of semantics and context to novel stimuli can give rise to the false recognition of unfamiliar people. *Neuropsychologia* 41, 538-549.
- Warrington, E.K. and James, M. (1967). An experimental investigation of facial recognition in patients with unilateral cerebral lesions. *Cortex* 3, 317-326.
- Warrington, E.K. (2004). Recognition memory test.

- Webster,M.J., Bachevalier,J., and Ungerleider,L.G. (1994). Connections of inferior temporal areas TEO and TE with parietal and frontal cortex in macaque monkeys. *Cerebral Cortex* 4, 470-483.
- Whiteley,A.M. and Warrington,E.K. (1977). Prosopagnosia: a clinical, psychological, and anatomical study of three patients. *Journal of Neurol Neurosurgery Psychiatry* 40, 395-403.
- Wilbrand,H. (1892). Ein Fall Seelenblindheit und hemianopsie mit sectionsbefund. *Deutsche Zeitschr.Nerveheil* 2 , 361-387.
- Williams,L.M., Brown,K.J., Das,P., Boucsein,W., Sokolov,E.N., Brammer,M.J., Olivieri,G., Peduto,A., and Gordon,E. (2004). The dynamics of cortico-amygdala and autonomic activity over the experimental time course of fear perception. *Brain Res.Cogn Brain Res.* 21, 114-123.
- Williams,M.A., Moss,S.A., and Bradshaw,J.L. (2004). A unique look at face processing: the impact of masked faces on the processing of facial features. *Cognition* 91, 155-172.
- Winston,J.S., O'Doherty,J., and Dolan,R.J. (2003). Common and distinct neural response during direct and incidental processing of multiple facial emotions. *Neuroimage* 20, 84-97.
- Winston,J.S., Vuilleumier,P., and Dolan,R.J. (2003). Effects of low-spatial frequency components of fearful faces on fusiform cortex activity. *Current Psychology* 13, 1824-1829.
- Winston,J.S., Henson,R.N., Fine-Goulden,M.R., and Dolan,R.J. (2004). fMRI-adaptation reveals dissociable neural representations of identity and expression in face perception. *J.Neurophysiol.* 92, 1830-1839.
- Wiser,A.K., Andreasen,N., O'Leary,D.S., Crespo-Facorro,B., Boles-Ponto,L.L., Watkins,G.L., and Hichwa,R.D. (2000). Novel vs. well-learned memory for faces: a positron emission tomography study. *J.Cogn Neurosci.* 12, 255-266.
- Wiskott,L., Fellous,J.-M., Kruger,N., and von der Malsburg,C. (1997). Face recognition by elastic bunch graph matching. *IEEE Trans.of Pattern Analysis and Machine Intelligence* 17, 775-779.
- Wojciulik,E., Kanwisher,N., and Driver,J. (1998). Covert visual attention modulates face-specific activity in the human fusiform gyrus: fMRI study. *J.Neurophysiol.* 79, 1574-1578.
- Wolland,A.M. and Hagelsteen,J.H. (1991). [Prosopagnosia. A rare disorder of visual perception]. *Tidsskr.Nor Laegeforen.* 111, 3505-3506.
- Worsley,K.J. and Friston,K.J. (1995). Analysis of fMRI time-series revisited - again. *Neuroimage* 2, 173-181.
- Yamane,S., Kaji,S., and Kawano,K. (1988). What facial features activate face neurons in the inferotemporal cortex of the monkey? *Exp.Brain Res.* 73, 209-214.
- Young,A.W. (1992). Face recognition impairments. *Philos.Trans.R.Soc.Lond B Biol.Sci.* 335, 47-53.
- Young,A.W., Humphreys,G.W., Riddoch,M.J., Hellawell,D.J., and de Haan,E.H. (1994). Recognition impairments and face imagery. *Neuropsychologia* 32, 693-702.